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INTUSSUSCEPTION

A Review of Experience at the Massachusetts General Hospital, 1937–1951

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BOSTON

SINCE Codman[1] reported observations on 27 cases of intussusception early in this century, no specific review of consecutive cases has been reported from this hospital. A study of the experience during the fifteen years from 1937 through 1951 reveals 60 cases of this disease. These included 2 cases of recurrent ileocolic intussusception in patients previously treated here, and 5 cases of intussusception observed as an incidental finding at laparotomy performed for another indication. The following review discusses the 53 patients who were treated at this hospital primarily for acute intussusception. The age distribution of patients (Table 1) makes it apparent that the number of older patients is not in accordance with the recognized rare incidence[2] in adults, but reflects the preponderance of adults in the population of this hospital.

> The general appearance of the child is, I feel sure, frequently the cause of mistakes in diagnosis. Children in the early hours (six to twelve) do not look sick. . . . The child at the very first onset turns pale, looks very ill, screams, but it is wonderful how quickly some of them recover themselves . . . . If you want to avoid falling into error, I advise you always to listen to the story of the mother when she comes to you with her baby . . . . The baby was quite well, when suddenly (often just after taking the breast or after passing a motion) it screamed or cried out, turned pale, and soon vomited. The screaming continued for a short time, and the pallor soon disappeared, but the child seemed uneasy and got frequent attacks of pain. . . .

It is disturbing to find, however, in the histories of 5 of the 6 younger patients with gangrenous intussusception in the present series, that there was no mention of pain; it was also absent in 3 cases of nongangrenous intussusception in this age group. In the acute cases in adults, there were none without pain, although it was not described as being intermittent or colicky as frequently as in children. The duration of symptoms is definitely more prolonged in this age group, half the patients giving a history of nine days or longer. This characteristic of intussusception in adults is emphasized by Eliot and Corscaden.[4] Recurrent attacks of severe pain, suggestive of chronic intussusception, were present in only 2 children, but occurred in about a quarter of the adults.

Nausea and vomiting were noted in nearly all the children, but in only half the adult cases. A history of melena was absent in half the children and in nearly all the adults. This symptom, usually alarming to parent or patient, was elicited far less frequently than other authors[2, 5-7] have reported.

TABLE 1. *Analysis of Acute Cases of Intussusception.*

AGE GROUP	MALE PATIENTS	FEMALE PATIENTS	FATAL CASES	RESECTIONS	DEATHS AFTER RESECTION	TOTALS
Children (0-12 yr. of age)	24	14	3	5	1	38
Adults (13-76 yr. of age)	9	6	3	13	1	15
Totals	33	20	6	18	2	53

SYMPTOMS

Pain, usually intermittent and colicky, was the dominant symptom in two thirds of the patients in the younger age group. In half the histories, the actual words "doubling up" appeared. Codman considered this characteristic history of pain most significant, especially when it is accompanied by a relative state of well-being between attacks. To emphasize this point, we believe, as Codman did, that the excellent description so clearly set forth by Clubbe[3] bears repetition:

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Signs

Most of the children appeared well when not in pain; the adults, in general, more truly reflected the abdominal disease. Resistance of the abdominal wall in the absence of a mass was the most constant finding in all age groups, occurring in two thirds of all cases. An abdominal mass was palpable in half the children but in only a third of the adults. Most other observers have noted a mass more frequently.[2, 5-7] A mass was noted on rectal examination in 4 children and 2 adults.

Laboratory Data

White-cell counts and hemoglobin determinations were of little value in diagnosis or prognosis. Guaiac-positive rectal contents were obtained in about half the children. In adults, the test was done infrequently and was usually negative.

X-Ray Findings

We have used plain abdominal films and barium-enema x-ray examinations as a diagnostic aid more regularly than is generally reported; half the children and all but 3 of the adult patients had both. In a third of these patients a definite diagnostic suggestion of intussusception was obtained by plain abdominal films with absence of a cecal gas shadow, often associated with a soft-tissue mass. Dilated loops of bowel usually occurred only late in the disease. Barium enema has proved a valuable diagnostic aid in this hospital, where the disease is infrequently encountered, and in only 1 enterocolic case was the examination misinterpreted as negative preoperatively. A false sense of security can be gained, however, if the lesion involves only small bowel.

Delay in Diagnosis

In 4 children surgery was delayed longer than twenty-four hours; underestimation of the history in the presence of relatively normal physical findings was the main cause. Two fatal gangrenous cases in this age group were not diagnosed before death because of severe concomitant disease — typhoid fever and glomerulonephritis with anasarca, respectively.

The greatest delays in diagnosis occurred in adults. Doubtless the diagnosis often was not considered, but two factors seem to play a part in this delay. Since in many adult cases the lesion was located in the small bowel, barium-enema examination was of no help. Secondly, intussusception is not usually associated with complete bowel obstruction until the process has been present for some time. These patients often improved on intestinal intubation, definitive therapy being delayed until gangrenous or completely obstructed bowel developed. The plain x-ray film of the abdomen was of little help until these events occurred.

Pathology

The types of intussusception encountered in this series are summarized in Table 2.

These pathological types are similar in distribution to those reported by others.[2, 6, 8] A relatively large percentage of enteric forms proved to be gangrenous, especially in adults. Most nongangrenous lesions were reducible in children, but there were no reducible lesions in adults. There were 5 cases of perforation in gangrenous lesions in adults.

No local cause for intussusception was found in 29 cases in children and in 6 adults. Eight children exhibited a markedly mobile cecum, a factor that has been considered of definite importance by several authors.[1-3, 9] As an associated finding, 14 of the children showed significant mesenteric lymphadenopathy. One case of intussusception was associated with typhoid fever; several reports of this coexistence have been made.[4, 9, 10] The two definite local causes in children were Meckel's diverticulum and duplication of the ileum. Two adult patients had Meckel's diverticulum, and 6 had mucosal polyps, 1 of which showed low-grade malignant change.

In 1 child, there were two separate jejunal intussusceptions, a third ileocecal type having been observed to reduce during diagnostic barium-enema examination. Multiple intussusception, though rare, may be considered a rationale for laparotomy.[6, 11] One adult case of jejunal location was retrograde — an occurrence rarely reported.[12]

Many authors have related the state of the bowel to the duration of symptoms.[2, 3, 5] Although this correlation is generally valid in the adults, our findings in children are at variance with this observation. Of 5 gangrenous cases in the younger age group, 3 had a total duration of symptoms of twenty-

Table 2. *Acute Cases of Intussusception Classified According to Location and State of Bowel.*

Location	Children			Adults	
	Simple cases	Irreducible cases	Gangrenous cases	Irreducible cases	Gangrenous cases
Enteric	3	—	1	1	7
Enterocolic	28	1	5	3	3
Colic	—	—	—	1	—

four hours or less; only 2 of the 10 gangrenous cases in adults had as short a duration of symptoms. Conversely, there were 16 nongangrenous cases in the series, evenly distributed among both age groups, in which symptoms had been present longer than seventy-two hours. It seems reasonable to conclude from our experience that the location of the intussusception, especially its occurrence in the narrow intussusceptum of the small bowel, bears a more direct relation to the state of the bowel than the duration of symptoms does. At present there is, however, no means of identifying a gangrenous lesion preoperatively. An assumption cannot be made that because of a short history of symptoms gangrene is unlikely.

Therapy

Our treatment has been entirely surgical; as yet we have not used hydrostatic methods, except in 3 cases in which reduction occurred incidentally during diagnostic barium-enema examination. Of the 53 acute cases in the series, operations specifically designed to cure the disease were performed in 49. Of the patients not subjected to operative therapy 2 were children who had no ante-mortem diagnosis, as mentioned above under delay in diagnosis. Two adults were operated on shortly before death. One had refused earlier operation, and another was considered no candidate for resection of an irreducible intussusception because of cirrhosis with ascites.

Among the 49 cases treated by operation were 36 children. In 3 of these patients the enterocolic intussusception was found to have been reduced when preoperative barium-enema examination was performed; 1 had a double intussusception of the jejunum still present and requiring reduction. In 28 cases simple reduction was accomplished at laparotomy. There were no deaths in the patients with nongangrenous intussusception. During the period from 1918 to 1927, in this hospital, the mortality following reduction was 50 per cent.[13] The present safety of this method of treatment, which has been appreciated by others,[5] must reflect better preparation and supportive care of patients, for antibiotic therapy was used in only 3 cases.

Concomitant appendectomy was performed in 26 of the 31 children who underwent laparotomy for uncomplicated reducible intussusception. This added no risk, but there is no indication that it will prevent enterocolic intussusception, since recurrences developed in 1 of these cases and in another in which appendectomy had not been done. One enterocolic intussusception occurred a year after appendectomy for acute appendicitis. Plication of a mobile cecum and fixation to the parietes were performed in 2 cases, 1 of which was a recurrent intussusception; the other closely followed it in the hands of the same surgeon.

In gangrenous or irreducible cases we have routinely carried out resection and primary anastomosis. In all but 1 case, open rather than aseptic technics have been used. Five children and 13 adults comprised the group in which resection was necessary. Of the 5 children, 4 had gangrenous bowel, and 1 desperately ill infant operated upon in the first year of this series died. In retrospect, inadequate control of fluid balance may have contributed to this patient's death. In succeeding years, in our limited experience, these patients have done well after resection and anastomosis, 3 being two years of age or under. We realize that surgeons with a wider experience have abandoned primary anastomosis because of its prohibitive mortality.[3, 6] However, McLaughlin,[14] in a review of 200 cases of resection appearing in the literature from 1907 to 1947, reported a 67 per cent mortality with primary anastomosis and an 87 per cent mortality with enterostomy, and Dennis[15] has attracted attention by his 7 successful cases of primary aseptic anastomosis. Gross and Ware,[6] in contrast, have abandoned this procedure, and by using a modified Mikulicz resection report a reduction in mortality to 9 per cent over the last nine years. A similar technic has been employed successfully by Ravitch and McCune.[5]

In adults there were 13 resections with primary anastomosis. The oldest patient in this group was seventy-six years of age. Postoperative complications included minor wound sepsis in 2 cases and pelvic abscess in two cases. Aseptic anastomosis and antibiotic administration did not prevent these complications. Nonfatal pulmonary embolism occurred in 2 cases. There was 1 death in a fifty-five-year-old adult who was operated upon twelve days after the onset of symptoms, having been treated at this hospital by intestinal intubation for seven days. On the eighth day after resection with anastomosis of the ileum to the ascending colon for a gangrenous perforated intussusception, a leak developed at the suture line. Despite, or because of, a nonfunctioning ileostomy, progressive infection and cachexia occurred, and the patient died on the forty-third postoperative day.

Summary and Conclusions

Intussusception, as encountered in a general hospital, occurs at any age. A characteristic history of colic — the finding of abdominal resistance or a mass — and studies with plain and barium-contrast x-rays are of greatest help in diagnosis. However, x-ray examinations are not useful in enteric forms and may give a false sense of security. Difficulty in diagnosis is frequently encountered, especially in older patients. Intussusception is not obstructive until late in the disease — a factor that accounts for delay in diagnosis in many adults.

The treatment in our hands has been entirely surgical, with satisfactory results in the uncom-

plicated cases. Laparotomy with manual reduction, accompanied by concomitant appendectomy, has produced no deaths and few complications. Gangrenous and irreducible bowel has been resected and continuity restored by primary anastomosis in all patients in whom definitive therapy was possible. Although our experience with resection is small, this procedure has been well tolerated by the patients.

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THE MURMUR OF PERIPHERAL ARTERIOVENOUS FISTULA*

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THE detection of a continuous murmur with systolic accentuation is of the highest significance in the diagnosis and in the location of the site of an arteriovenous fistula. It is therefore appropriate to emphasize certain characteristics of the murmur that may increase its usefulness as a physical sign. The study of patients with arteriovenous fistula by auscultation has been supplemented by visual registration of the murmurs through the use of a microphone connected to the phonocardiographic channel of a multiple-channel electrocardiograph. Several phonoangiograms thus obtained are reproduced in this report. Simultaneous tracings of the pulse wave or the electrocardiogram are shown to elucidate the timing of the murmurs.

Observations

Character of the Murmur

The murmurs heard directly over the fistulas are high pitched and continuous — that is, they extend through the entire cardiac cycle (Fig. 1). The difference in frequency and amplitude between their systolic and diastolic portions is often so distinct, however, that the murmur is sometimes described as having a to-and-fro character.

The systolic accentuation is a more prominent feature than is generally appreciated, the degree of accentuation varying from case to case. Moreover, even the most obviously continuous murmur can be converted to a systolic one by obstruction of the effluent vein. In the patient in whom this change is demonstrated in Figure 1, the venous pressure in a superficial vein near the fistula was increased from 15 mm. of mercury to a level of 36 mm. of mercury by compression of the outgoing femoral vein. The arterial blood pressure measured in the arm was 110 systolic, 75 diastolic. The rise in venous pressure lowered the arteriovenous-pressure gradient to a point where the velocity of flow from artery to vein during diastole was apparently too low for vibration production. The site of the fistula in this patient is demonstrated in the angiogram illustrated in Figure 2.

The murmur of arteriovenous fistula is usually loud, the intensity being roughly proportionate to the size of the fistula. In our experience no fistula has been disclosed by x-ray angiography when auscultation has failed to reveal a murmur. On the other hand, fistulas of minute proportions can quite obviously exist without giving rise to a murmur.

A palpable thrill has accompanied the murmur in all but small, deep-seated fistulas. This is based upon the presence of some vibrations within the frequency range of tactual perception.[1] Undoubtedly, the high intensity of the vibrations aids in their appreciation. Although we have made no special study of thrill perception our experience with arteriovenous fistula leads us to agree with the conclusion reached by Counihan, Rappaport and Sprague[1] for cardiac lesions: "The sensitivity of the fingers to vibrations in the range of (cardiac) murmurs is so far inferior to that of the ear that the

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elicitation of a (cardiac) thrill becomes a matter of academic curiosity and yields no information of diagnostic import that is not obtained by auscultation."

Location of the Murmur

Although the murmur is often heard over a wide area it is most intense directly over the fistula. When multiple fistulas are present multiple sites of great intensity may be expected. From its site of production in the fistula the murmur is often widely transmitted via the bones and along the vein leading out of the fistula. Effective bone transmission requires only that the fistula lie in apposition to some portion of the skeleton.[2] This is illustrated for an extremity in Figure 3, in which it may be noted that the murmur is louder over bones at some distance from the fistula than over the soft parts quite close to the fistula. Bone transmission is particularly helpful in the diagnosis of intracranial fistulas, the murmur usually being easily appreciated over the skull. In the same way, moreover, the murmur is transmitted to the patient's own ear.

Special significance attaches to the audibility of the murmur over the vein leading from the fistula. Here the murmur is intense and may be heard for a long distance proximally, sometimes all the way back to the heart. Two facts suggest that the murmur over the vein is only partly transmitted from the fistula, and partly generated within the vein through the mechanism of high-velocity flow. The first is that the systolic accentuation is often less pronounced over the vein than over the fistula (Fig. 1). The second is the great effectiveness of proximal compression of the vein in reducing the intensity of the murmur in that vessel (Fig. 1).

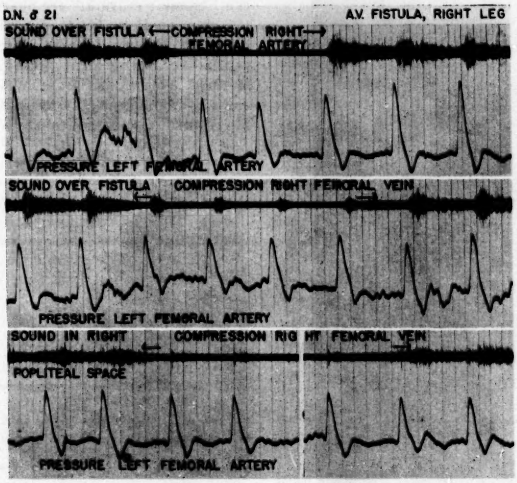
D.N. ♂ 21
A.V. FISTULA, RIGHT LEG
SOUND OVER FISTULA ←COMPRESSION RIGHT→ FEMORAL ARTERY
PRESSURE LEFT FEMORAL ARTERY
SOUND OVER FISTULA COMPRESSION RIGHT FEMORAL VEIN
PRESSURE LEFT FEMORAL ARTERY
SOUND IN RIGHT COMPRESSION RIGHT FEMORAL VEIN
POPLITEAL SPACE
PRESSURE LEFT FEMORAL ARTERY

FIGURE 1. *Tracings in Patient D. N.*

Upper tracing — the murmur disappears on arterial occlusion. The fistula is too small for this maneuver to lower the pulse rate.

Middle tracing — the murmur loses its diastolic vibrations on occlusion of the proximal vein.

Lowest tracing — the murmur is present over the popliteal vein and is greatly diminished by proximal venous occlusion. Persisting vibrations are entirely systolic in phase.

DISCUSSION

Mechanism of Murmur Production

The mechanisms of murmur production in vascular disease have been considered in detail in a previous paper.[3] In general, an increase in velocity of the blood stream and abrupt changes in vessel diameter are important vibration-inducing factors. The primary cause of the murmur in arteriovenous fistula is the extreme gradient from the high pressure level of the artery to the low level of the vein. This gives rise to a rapid flow through the fistula, with consequent vibration of the stream and sound production. The higher pressure gradient and

higher velocity existing in systole account for the accentuation in this phase. Although the gradient is less in diastole, it is adequate for continued vibration production, unless, as demonstrated, venous obstruction raises the pressure against which the arterial blood contends. That a systolic rather than a continuous murmur occurs under such conditions has been demonstrated for patent ductus arteriosus by Burchell[4] and by Myers et al.[5] Theoretically, the vein may vibrate and contribute to the sound, if the jet of blood from the fistula happens to be so directed as to strike against the venous wall. A third source of vibration is the rapidly coursing stream in the vein proximal to the fistula. Such a "high-velocity murmur" is engendered when the vein is distended close to its elastic limit by the unaccustomed quantity of blood under high pressure.

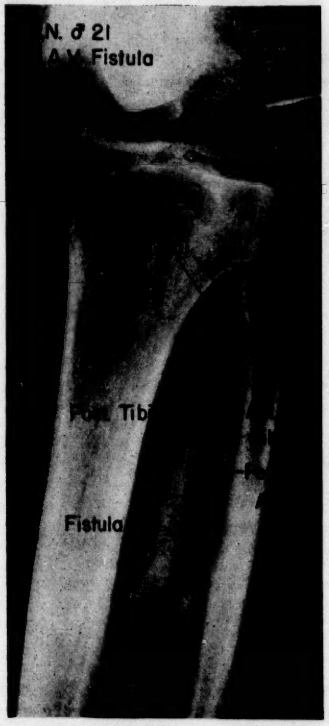

FIGURE 2. *X-Ray Angiogram in Patient D. N., Showing an Arteriovenous Fistula of the Posterior Tibial Vessels (Reproduced through the Courtesy of Lieutenant Colonel William S. Cornell, Murphy Army Hospital).*

The fistula, caused by a gunshot wound, was subsequently removed at operation, with disappearance of the murmurs reproduced in Figures 1 and 3.

Differential Diagnosis

No condition other than arteriovenous fistula, to our knowledge, gives rise to a peripherally produced continuous murmur with systolic accentuation. Similar murmurs are heard over the placenta, the thyroid gland in exophthalmic goiter and the bones in Paget's disease, but an arteriovenous-fistula-like arrangement presumably exists in each of these conditions. Care must be taken to rule out a cardiac origin of the murmur, since the bones can transmit such murmurs widely. Even when it is certain that the murmur is of peripheral origin one must rule out several other causes. The hum sometimes present over the internal jugular and other veins is a continuous murmur, but with a diastolic accentuation. Continuous murmurs may be heard over abdominal veins in patients with portal obstruction. Accentuation of this murmur occurs with a random timing, and usually lasts for several seconds. One may judge the murmur of arteriovenous fistula to be systolic, through failure to appreciate the diastolic portion, or because the murmur is in fact systolic, owing to obstruction of the outgoing vein. A systolic murmur must be differentiated from that caused by partial obstruction of the arteries, either intrinsic, as by arteriosclerosis, or extrinsic as by cervical rib — and from the murmur of arterial aneurysm, either true or false. Examples of the murmurs of most of the con-

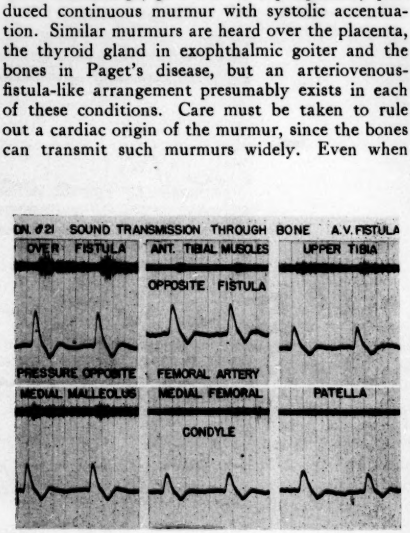

FIGURE 3. *Murmur Transmission through the Bones of the Limb in Patient D. N.*

The murmur is louder over the upper or lower tibia than over the nearby muscle.

ditions mentioned were given in the previous publication.[3]

Optical registration of the murmur with simultaneous electrocardiographic or pulse-pressure tracing is of considerable value in the study of a suspected case of arteriovenous fistula. The method offers an objective demonstration of the nature of the murmur, indicating whether it is continuous and whether there is systolic accentuation. It also offers a good means of demonstrating whether slowing of the heart rate occurs during compression of the fistula or of the entering artery (Fig. 4).

Auscultation in Location of the Fistula

The site of maximal intensity of the murmur almost invariably marks the location of the fistula. The existence of several sites of great intensity usually indicates the presence of multiple fistulas. Some uncertainty may arise in fistulas situated within the head, thorax or abdomen, in which the murmur is often best heard over the bony confines of the region.

One must keep in mind the frequent presence of a murmur over the outgoing vein far proximal to the entrance of a fistula; otherwise, the murmur may mistakenly be regarded as evidence of the existence of one or more fistulas at the proximal level. In cases of congenital origin, in which multiple fistulas are the rule, one may determine the level of the most proximally located fistula by finding that area where compression obviates the murmur along the vein (Fig. 4). This point was emphasized by Blumgart and Ernstene[6] in 1932 in reporting the very patient whose murmur is shown in Figure 4.

Conclusions

The continuous murmur with systolic accentuation characteristic of arteriovenous fistula may be replaced by a purely systolic murmur when the effluent vein is compressed.

Registration of murmurs aids in the diagnosis of the fistula, and in the demonstration of cardiac slowing on arterial occlusion.

An intense murmur is often heard along the effluent vein for a long distance proximal to the site of the fistula, and should not be mistaken as indicating the presence of proximally located fistulas.

No fistula large enough to be visualized by x-ray angiography has failed to give an audible murmur. The absence of a murmur, on the other hand, has not ruled out minute fistulas.

Bony transmission of the murmur may allow it to be heard at some distance from the fistula. This is especially significant in fistulas located within the body cavities.

The murmur of arteriovenous fistula must be differentiated from murmurs of cardiac origin and from venous hums and, when apparently systolic in character, from partial arterial obstruction and arterial aneurysms.

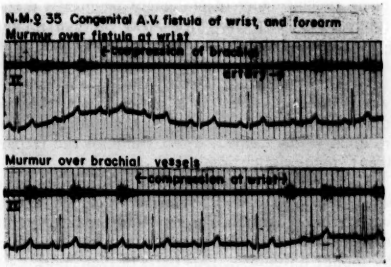

FIGURE 4. *Murmur over the Brachial Vessels and Fistula in Patient N. M. with Congenital Arteriovenous Fistulas of the Wrist and Forearm.*

This is the patient previously reported by Blumgart and Ernstene.[6] Proximal-artery compression causes disappearance of the murmur and slowing of the heart rate, from the original rate of 72 to 63. The murmur over the effluent vein all but disappears on compression of the distal fistula. The small groups of persistent systolic vibrations are apparently caused by the entrance of blood from the smaller fistula of the forearm.

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MALIGNANT NEOPLASTIC DISEASE DISCOVERED IN CHEST X-RAY SURVEYS*

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AN INCREASING number of publications stress mass x-ray surveys as the best method for the early detection of intrathoracic cancer. This study records our experience concerning the diagnosis and incidence of malignant neoplastic disease found in the course of chest x-ray surveys designed primarily for tuberculosis case finding. The material consisted of surveys conducted by the New York City Department of Health during the calendar years 1949 and 1950. All patients whose survey films showed the need for further work-up were recalled to the Central Chest Clinic of the Department for examination.

The surveys were organized on an occupational or on a regional basis; the former included a wide variety of occupational groups, and the latter represented unselected participants in surveys conducted by mobile units in various parts of New York City. In some of the surveys participation was compulsory, — for example, as a prerequisite to employment, — whereas in others it was voluntary. Generally, the initial survey film was a 70-mm. photofluorogram taken with the patient clothed. The survey films were interpreted twice but not independently, the result of the first reading being available to the second reader. As a rule, the second reader was a senior member of the staff, who reviewed and, whenever necessary, corrected the first interpretation.

Since the surveys were done in various parts of New York City and all persons recalled examined at the Central Chest Clinic, re-examination necessitated fairly long traveling for many patients. This factor may have accounted for the lack of co-operation in some cases.

Minimum work-up on first clinic visit consisted of history, physical examination, fluoroscopy and full-size x-ray films. Facilities for the following additional procedures were available at the clinic: Bucky film and tomography; skin testing with tuberculin, histoplasmin and coccidioidin; examination of sputum and gastric contents for tubercle bacilli by concentration and culture; sputum examination for fungi; and blood serologic tests. No provision was made for home visits by Health Department nurses or social workers in nontuberculous conditions. It was a definite drawback that sputum examination for tumor cells could not be performed at the Central Chest Clinic; specimens collected for this purpose could be submitted by the patient at another Health Department clinic only once weekly, which made examination of several specimens impracticable. For other examinations, such as bronchoscopy, aspiration of pleural fluid, biopsy and search for a possible primary tumor in another organ, patients had to be referred to private physicians or hospitals. Whenever a patient had a private physician, a full report of the clinic findings was sent to him, together with recommendations for further diagnostic procedures and management. Patients who did not have or could not afford a private physician were referred to the outpatient departments, usually the tumor clinics, of different voluntary or municipal hospitals, where admission to the ward was arranged.

An attempt was made to maintain contact with outside physicians and hospitals throughout the patients' illness. As far as possible, the patients were followed up to the time of this writing (May, 1952), the period of observation ranging from sixteen to forty months.

The group covered by this study consisted of 228,375 persons, almost all over fifteen years of age, who received survey x-ray examinations between January 1, 1949, and December 31, 1950. The largest individual survey comprised the entire professional and auxiliary personnel of public and parochial schools in New York City. This survey was mandatory and was heavily weighted by middle-aged and elderly females: out of a total of 45,051 persons in this group, 71.9 per cent were women, 47.3 per cent of whom were forty-five years and over. In the remainder of the survey population there was an approximately equal number of males and females; roughly 65 per cent were below the age of forty-five.

Out of the total of 228,375 persons surveyed, 184 (0.8 per 1000) were suspected of having malignant neoplastic disease of the chest. One hundred and sixty-three were so labeled on the initial 70-mm. film, and the other 21 were recalled with some other tentative diagnosis and considered suspicious for tumor during their work-up in the clinic.

In 3 persons whose survey films had been read as negative, subsequent information revealed the presence of significant chest anomalies (2 pulmonary metastases, and 1 hilar mass). Review of the survey films revealed findings that should have been interpreted as suspicious for malignant neoplastic disease and led to a recall. Although we were aware that cancer could simulate roentgenographically a multitude of pulmonary conditions, the following abnormalities on the survey film were considered to carry a sufficiently high probability of neoplasm to

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warrant recall of the individual as a tumor suspect: single circumscribed round or ovoid shadows of varying size and density, 58 cases; multiple (two or more) round circumscribed shadows, 9 cases; dense, more or less homogeneous parenchymal shadows of irregular shape, 10 cases; x-ray changes suggestive of atelectasis, 5 cases; widening of the mediastinal shadow, or densities adjacent to the mediastinal structures, 72 cases; status post mastectomy, with pleural effusion or parenchymal shadows, or both, 6 cases; and rib abnormality suggestive of neoplasm, 3 cases. No cases of localized emphysema or miliary nodulation were seen in this series.

After admission to the clinic it was believed that protracted diagnostic procedures should be avoided as much as possible. No attempt was made to prove or disprove tuberculosis by means of sputum or gastric cultures in a pulmonary lesion suspicious of neoplasm. The observation of such a lesion by serial x-ray films over a period of months for evidence of roentgenologic change was considered to be definitely contraindicated. It was believed that "watchful waiting" in such cases might be a highly dangerous procedure, since stability on x-ray examination even for prolonged periods does not disprove cancer, and roentgenologic evidence of progression may already indicate inoperability. At present, early exploration of the chest offers the only possibility of early diagnosis and early treatment in the majority of cases. As pointed out below, of the 21 cases of pulmonary neoplasm found, 15 were diagnosed on exploration only. Unless full-size x-ray films, tomograms, available previous films, positive sputum concentrates for tubercle bacilli or other specific findings quickly disproved the suspicion raised by the initial survey film and helped in establishing a definite or highly probable diagnosis of a nonmalignant condition, the case was considered an emergency and the patient was referred to a hospital with exploration in mind.

This radical approach crystallized more and more during the period covered by this study and was not consistently applied in all cases in the beginning. The present attitude developed as a consequence of the increasing safety of thoracic surgery and of the increasing awareness of the dangers of delay. This policy inevitably subjects a number of patients with nonmalignant conditions to the risk and discomfort of operation; however, with the present low operative mortality, it appears that less harm will be done in removing a nonmalignant lesion than in missing the resectable phase of a malignant tumor. It is fully recognized that in the individual case of a silent lesion, the decision whether or not to advise exploration may be very difficult and involves heavy responsibility. With the diagnostic tools at our disposal at present, a certain subjective and sometimes arbitrary element enters unavoidably into the evaluation of the potential malignancy of a lesion.

Table 1 gives the final classification of the 184 suspicious cases. Table 2 correlates the final classification with the initial survey findings in the 163 cases considered suspicious on the survey films.

Primary Malignant Neoplasm

Thirty cases of primary malignant neoplastic disease were found among the 184 persons with suspicious films. Three of them had been diagnosed previously. In 24 of the 27 previously unrecognized cases, the diagnosis was proved by histologic examination. In the remaining 3 cases, microscopical proof was lacking, but the clinical and roentgenologic course left little room for doubt regarding the diagnosis of malignant neoplasm. One of these 3 patients had marked bilateral widening of the mediastinal shadow, which decreased considerably in size after x-ray therapy. The 2 others apparently had bronchogenic carcinoma; 1 refused operation and received radiotherapy, which was followed by slight temporary improvement; in the second patient, age and general condition contraindicated surgical treatment. This patient died a year and a half after the survey film had been taken.

This discussion refers to the 24 histologically proved and previously unrecognized cases. Three patients were found to have Hodgkin's disease. Their survey films showed unilateral hilar densities or widening of the mediastinal shadow. Of the 21 pulmonary tumors, 7 (a third) were not suspected on the survey film. The findings in these cases were entirely uncharacteristic and resembled either basal pneumonitis or small, irregular, nonhomogeneous infiltrations in the upper lobes suggesting minimal pulmonary tuberculosis. In the remaining 14 patients with pulmonary tumor, recalled because of suspicious survey findings, the lesions in 6 appeared as single, round parenchymal shadows, in 4 as dense, homogeneous shadows (1 associated with pleural effusion) and in 5 as widening of the mediastinum

Table 1. *Final Classification of All Suspicious Cases.*

Classification		No. of Cases	Percentage
Primary pulmonary neoplasm		27	14.6
Hodgkin's disease		3	1.6
Metastases from extrathoracic cancer		20	10.9
Nonmalignant conditions		60	32.6
Tuberculosis	21		
Benign tumors (including rib tumors)	8		
Sarcoidosis (presumable)	5		
Nonspecific pulmonary changes*	8		
Cardiovascular abnormalities	6		
Changes of pleura and diaphragm	5		
Rib abnormalities	2		
Cancer excluded†	5		
No abnormal findings		16	8.7
Undetermined		58	31.6
Total		184	

*Includes nonspecific pneumonia, lipoid pneumonia, pulmonary fibrosis and cysts.

†No definite diagnosis established, but neoplasm excluded with reasonable certainty.

or masses adjacent to it. Two patients had x-ray changes suggestive of atelectasis.

Of the 21 patients with malignant pulmonary tumors, 13 were male, with an average age of fifty-eight and five-tenths years, and 8 female, with an average of fifty-three and five-tenths years. The higher proportion of females in our series as compared with most other statistics can be explained by the age and sex distribution of the school survey, as mentioned above, since 7 of the 8 females were schoolteachers.

Of the patients with Hodgkin's disease, 1 was male and 2 female; their ages ranged between twenty-six and thirty.

Ten of the 24 patients had no symptoms; their lesions were truly silent. In 12 patients symptoms were present, but mostly of a mild degree. In the symptomatic group, all patients with pulmonary tumor had cough; the other symptoms, in order of frequency, were expectoration (6 cases), blood-streaked sputum (3 cases), weight loss (3 cases), chest pain (2 cases), dyspnea (1 case) and asthenia (1 case).

Data on smoking habits are insufficient for evaluation in this series.

Abnormal physical findings were present in 7 cases and absent in 15; in 2 cases, no adequate record of physical findings is available. The abnormal signs noted were localized wheezing (2 cases), diffuse wheezing (2 cases), localized rales (1 case) and dullness and diminished breath sounds (2 cases); clubbing of fingers was found in only 1 case. Large, matted supraclavicular lymph nodes were present in 1 case of Hodgkin's disease. The differential diagnostic significance of a negative tuberculin test was illustrated by 1 patient, fifty years of age, who was subsequently proved to have carcinoma, in whom the negative reaction strongly influenced the decision to advise early exploration.

In the patients subsequently found to have malignant tumors, the information obtained from complete roentgenologic work-up was not substantially greater than that which was obtained from the survey film and did not permit the establishment of a definite diagnosis. Our experience fully confirms the lack of specific and reliable roentgenologic criteria for pulmonary cancer.

As described below, roentgenologic studies, including tomography, were often important in disproving the suspicion raised by the survey film and indicating a nonmalignant condition — for example, by demonstrating calcium deposits within the lesions. Tomography and x-ray films taken in different positions were also useful in localizing a lesion, but this was hardly of any help in differential diagnosis.

TABLE 2. *Correlation of Survey Findings With the Final Diagnosis.*

FINAL DIAGNOSIS	APPEARANCE ON SURVEY FILM							
	SINGLE ROUND SHADOW	MULTIPLE ROUND SHADOWS	HOMOGENEOUS PARENCHYMAL DENSITIES	CHANGES SUGGESTING ATELECTASIS	ABNORMAL MEDIASTINAL SHADOW	MASTECTOMY WITH COMPLICATIONS	SUSPECTED TUMOR OF RIB	TOTALS
Primary pulmonary cancer	6		4	2	5			17
Hodgkin's disease					3			3
Metastases from extrathoracic cancer	6	4	1		1	5		17
Tuberculosis	15	1			3			19
Benign tumors (including rib tumors)	2				3		3	8
Sarcoidosis (presumable)					5			5
Nonspecific pulmonary changes*	1		1	1	2			5
Cardiovascular abnormalities					5			5
Changes of pleura and diaphragm	1		1		2			4
Rib abnormalities	2							2
Cancer excluded†		1			4			5
No abnormal findings	7		1		8			16
Undetermined	18	3	2	2	31	1		57
Totals	58	9	10	5	72	6	3	163

*Includes nonspecific pneumonia, lipoid pneumonia, pulmonary fibrosis and cysts.
†No definite diagnosis established, but cancer excluded with reasonable certainty.

Whenever possible, an attempt was made to obtain chest x-ray films taken prior to the suspicious survey film. Such films could be obtained in 11 of the 24 proved cases. Seven of the old films did not show any abnormal findings. The interval between the negative film and the suspicious survey x-ray film was a year in 1 case, two to two and a half years in 5 cases and 4 years in 1 case.

In 1 case the presence of a lesion on the old film was questionable. In another, a survey film taken two years previously had been read as negative. On review, this film revealed an oval density adjacent to the diaphragm. This density was smaller but corresponded to the tumor picked up on a similar survey film two years later. It is interesting to note that this patient had an adenocarcinoma that was operable. The regional lymph nodes were not involved.

In 2 cases roentgenologic anomalies on previous films had been interpreted as minimal tuberculosis; both patients had small, irregularly outlined infraclavicular infiltrations; both had been discharged from further observation as "apparently cured" about two years before the suspicious survey film. Neither of them had positive sputum at any time.

The tuberculin test gave a positive result in 1 case; it had not been done in the other. In both cases the initial survey films showed a roundish shadow, considerably larger, denser and better circumscribed, at the site of the previous involvement. At first, both patients were thought to have active progressive tuberculosis. Eventually, the presence of bronchogenic cancer was proved, by exploration in 1 case and by the finding of malignant cells in the pleural fluid in the other.

Of the 21 pulmonary tumors, 18 were of the peripheral and only 3 of the central type. This distribution is not surprising in survey material, since the central lesions are more likely to cause severe symptoms early in their course and to be seen first in doctors' offices and hospitals. It is to be emphasized that 4 of the peripheral tumors were very small when first seen, not exceeding 1.5 cm. in diameter.

The diagnosis of the 21 primary malignant tumors of the lung was definitely established by surgical exploration in 15 cases, by bronchoscopic biopsy in 2 cases and by demonstration of malignant cells in the pleural fluid in 4 cases. In the 3 cases of Hodgkin's disease the diagnosis was made by biopsy of a peripheral lymph node.

The 4 cases with malignant cells in the pleural fluid were clearly unsuitable for exploration. Another patient, in whom the diagnosis was made by bronchoscopy, was not operated upon because of his age and general condition. Thus, a total of 16 patients was subjected to exploratory thoracotomy. The interval between the survey film and surgical intervention was two or three months in 5 cases, four or five months in 5 cases, six to twelve months in 2 cases and thirteen to nineteen months in 3 cases. In 1 case resection was performed a month after the survey film; however, a tentative diagnosis of bronchogenic carcinoma had been made by the patient's private physician eight months previously.

Analysis of the delays shows that time was often lost at the following points: delay between survey film and Central Chest Clinic admission, which was due to disproportion between the volume of survey films taken in a short time and clerical and medical personnel available at the clinic; delay between Chest Clinic admission and hospital referral, which was due to poor co-operation of the patient; and delay between admission to the tumor clinic of a hospital and exploration.

Of the 16 patients who underwent exploration, 12 were found to have operable lesions; pneumonectomy was performed in 6 patients, lobectomy in 5, and local excision in 1. In an additional case, pneumonectomy was performed as a palliative procedure, though the tumor had spread beyond the lung. In this small series, no correlation could be demonstrated between operability and the time elapsed between survey film and exploration.

Of the 17 tumors examined microscopically (16 explorations and 1 bronchoscopy), 9 were found to be squamous-cell carcinoma, 5 adenocarcinoma, 2 undifferentiated carcinoma and 1 a hemangioendothelial sarcoma.

Three patients died after operation: 1 of postoperative shock, 1 of pulmonary embolism and 1 of bronchopleural fistula and uncontrollable infection.

Metastatic Tumors

Twenty cases of intrathoracic metastases were found. In 9 of these the diagnosis was already obvious on the survey film, which showed either multiple round densities in the lung fields or status post mastectomy with pleural effusion or pulmonary infiltrations, or both. The primary tumor had been in the breast in 12 cases, in the kidney in 2 and in 1 case each in 1 of the following organs: cervix, colon, rectum and testicle. In 2 cases the site of the primary tumor was unknown. All but 1 of the patients with metastatic disease were working at the time of the survey x-ray examination. In 11 of the 20 patients, the presence of intrathoracic metastases had been unknown to the patients' own physicians. In 8 of these 11 cases, the primary tumor had been previously treated with operation or radiotherapy; the intervals between treatment of the primary tumor and the abnormal survey film were one year in 1 case, one or two years in 2, three or four years in 4, and 5 years in 1. In our series of metastatic lesions, there was only 1 case of a solitary pulmonary shadow after mastectomy in which operative removal could be considered.

Nonmalignant Conditions

In 60 cases, the suspicious x-ray findings were found to be due to nonmalignant conditions (Table 1).

Within this group the largest number (21 cases) were proved or probable tuberculous lesions. In 5 of these a calcified primary focus had appeared on the survey film as a softer circumscribed shadow suggestive of tumor. In 1 case of peripheral, round density, the tuberculous etiology was demonstrated at resection only. In 5 cases the diagnosis of tuberculosis was established by positive bacteriologic results. In 1 case with multiple round densities on the survey film, tomography revealed a thin-walled apical cavity. In the remaining cases, calcium deposits were seen within the lesions on the full-size film, Bucky film or tomogram. In the differential diagnosis of this group, tomography proved particularly useful in demonstrating small calcifications within lesions that appeared homogeneous on the standard film. All these patients had a positive tuberculin reaction. It must be admitted that in these cases of silent, partially calcified lesions there is no exact scientific proof of tuberculous etiology. Some of them, for instance, may be hamartomas.

For practical purposes, these lesions were considered as nonmalignant, and exploration was not advised.

Benign tumors of the lung and mediastinum were found in 5 cases; 3 of these were resected and proved to be adenoma, neurofibroma and chondroma, respectively. In the fourth case with a large, round, well defined shadow in the paravertebral gutter, previous films had demonstrated the same density five years previously. It was believed that the diagnosis of neurofibroma could be made with reasonable certainty. The fifth patient had a large lobulated mass containing many calcifications, some of them resembling teeth, and a diagnosis of dermoid cyst seemed highly probable. This mass had appeared fairly homogeneous on the survey film. Of the 3 detected rib tumors, 2 were resected and found to be benign.

Among the remaining nonmalignant cases, 1 deserves special mention: this patient with a large, round mass on the survey film was found to have extensive bilateral bullous emphysema. The round shadow represented one such bulla filled with fluid.

Among the cardiovascular abnormalities, 2 were large syphilitic aneurysms producing a tumor-like appearance on the survey films.

One patient had a large, well defined rounded shadow in the right cardiophrenic angle, which had not been seen on x-ray films taken six years previously; on resection this proved to be a pericardial cyst.

In 5 cases no definite diagnosis was established; however, all available evidence appeared to exclude cancer. In 1 case with x-ray findings suggestive of metastases, lung biopsy revealed nonspecific inflammatory changes of undetermined etiology; in another case an unexplained abnormality of the mediastinal outline disappeared spontaneously. In the other cases, the diagnostic possibilities rested among several nonmalignant conditions; for their exact diagnosis, exploratory operation or other major procedures did not seem indicated.

Sixteen patients with suspicious survey findings did not have any abnormality on the full-size film. The suspected shadows had apparently been due partly to clothing or artefacts and partly to vascular shadows that had simulated significant lesions on the 70-mm. film but appeared to be within normal limits on the standard x-ray film.

Undiagnosed Cases

In 58 patients, a third of all those suspected of tumor, a definite diagnosis had not been established in the period between the survey film and the writing of this paper. Thus, an unknown number of malignant conditions remains undetected in this group. These 58 cases can be divided into two main groups: 11 cases in which surgical exploration was not advised, because the lesions were not considered amenable to operation (for example, bilateral hilar masses), because the possibility of cancer, though not excluded, appeared extremely remote, or because the patient's age and general condition precluded any major procedure; and 47 cases in which the lack of a definite diagnosis in the presence of a suspicious intrathoracic lesion was due to poor co-operation of the patients and unawareness and conservative attitude of their private physicians, resulting in incomplete work-up.

The large number of patients in the second group is particularly significant. In spite of intensive efforts of the clinic staff, it was often impossible to obtain co-operation for clinic attendance and even minor diagnostic procedures in these mostly asymptomatic patients. Twenty-nine disappeared entirely from clinic follow-up study. Nine others, after having received a fairly complete but inconclusive work-up, refused exploratory thoracotomy. In an appreciable number of cases, the obstacle to a definite diagnosis was found in the attitude of the private physician, who refused to be impressed by the presence of an undiagnosed x-ray shadow in a symptom-free and healthy-appearing patient. These physicians saw no need even for the preliminary tumor work-up, and showed great reluctance to attribute any significance to these silent lesions; thus the stage when a decision concerning exploration could be made was not even reached. Other physicians objected to exploration in patients with no significant medical contraindication to operation, although preliminary diagnostic work-up had failed to rule out cancer.

Discussion

In the absence of a biochemical test for cancer, mass x-ray surveys are at present the best means of detecting intrathoracic malignant neoplastic disease in its earliest stages. Our experience demonstrates the problems involved in diagnostic work-up and management of patients with findings suspicious of tumor in chest x-ray surveys. Our yield of 30 cases of primary cancer among 228,375 persons (roughly 1 per 10,000) corresponds to the figures found by other workers.

With the therapeutic methods available at present, the early detection of malignant pulmonary tumors, especially bronchogenic carcinoma, is of greater practical significance than the discovery of cases in the lymphoblastoma group. The following discussion is limited to the malignant pulmonary tumors.

Of the newly discovered 21 cases, 16 could be subjected to exploration, and 12 were found to have operable lesions. This series demonstrates once more that cases found on routine screening are by no means all in the early and curable stage, nor are they all asymptomatic. This observation, however, does not negate the value of survey detection; although even small and silent tumors may be beyond the possibility of surgical cure, it is true that routine screening will reveal more lesions in an early and

resectable stage than examination of patients seeking medical attention because of symptoms.

In a discussion of the value of early detection of bronchogenic carcinoma, it must be kept in mind that long-term results are still extremely poor, even in cases that seemed to be curable at the time of operation. According to available statistics, five-year survivals are recorded in a very small percentage of patients. However, to date no long-term postoperative follow-up study is available in a significant number of patients with small silent lesions detected on survey. As described by Overholt, the situation found on operation of such silent tumors appears to be considerably more favorable than in symptomatic patients; however, his patients were operated on too recently for long-term evaluation.

To obtain the maximum benefit from survey detection, the interval between survey film and diagnosis should be reduced as much as possible. In the vast majority of peripheral lesions detected on survey, cancer can be suspected but not confirmed by roentgenologic criteria, none of which have specific diagnostic value; clinical work-up, bronchoscopy and cytologic examination of the sputum are apt also to give inconclusive results in such cases. Therefore, surgical exploration of the chest should be performed in all cases in which malignant neoplasm cannot be excluded rapidly. With this policy, the removal of nonmalignant lesions is unavoidable, but the comparative safety of present-day thoracic operations makes this a smaller risk than delay or omission of surgical intervention in a malignant lesion.

The number of metastatic tumors seen in this series is almost as great as that of primary tumors. The 8 cases with not previously known intrathoracic metastases following treatment of a primary tumor elsewhere point to the need for inclusion of chest x-ray examinations at regular intervals in the follow-up study of cancer patients. Although the early discovery of metastasis is often of little practical significance for the welfare of the patient, the recognition of this condition with its prognostic implications may be an important factor in planning for the future of the patient and his family.

The large number of undiagnosed cases in this series (about a third of all suspicious cases) is striking and somewhat discouraging. In these cases the effort and expense of the survey were completely wasted. In most of them the diagnosis remained undetermined because of poor co-operation of the patient or unawareness and conservative attitude on the part of the private physician. In contrast to the tuberculous, the person suspected of having cancer is not subjected to any pressure from the community to obtain diagnosis and treatment.

The efficacy of cancer detection by chest x-ray surveys could be improved in various ways. The ratio of tumors found to persons surveyed could be increased by better selection of the survey population. In view of the high incidence of bronchogenic carcinoma in men over forty years of age, it appears desirable to concentrate the available facilities on this group, especially since it is the same group in which tuberculosis is quite prevalent at present. In practice, it is not easy to arrange surveys in such a way that they will cover a significant segment of the older population. Young people are prevalent in most occupational groups and appear to participate in community surveys to a larger extent than the elderly. Perhaps present attempts to perform x-ray examinations on all patients admitted to general hospitals will reach a larger number of elderly people. Obviously, any extension of survey work, in number of persons examined and in frequency of re-examination of the same groups, is bound to increase the number of tumors found.

In an attempt to improve co-operation of persons with suspicious findings, clinics should be conveniently located and open after working hours. The medical staff should be large enough to give each patient sufficient time and attention; whenever possible, a patient should be seen by the same physician on each clinic visit. The help of trained social workers should be utilized.

As far as improvement in diagnostic methods is concerned, it appears desirable to expand facilities for cytologic examination of the sputum in clinics doing survey follow-up work. Close liaison between the survey follow-up clinic and the tumor clinic of a hospital should eliminate delay in arranging for bronchoscopy and exploration.

Finally, to improve the result of chest x-ray surveys, further education of practicing physicians and of the general public appears necessary. In the course of this study and in routine work in the chest clinic, we came to realize that a not insignificant number of physicians are unaware of the potential seriousness of silent intrathoracic lesions. They are apparently not familiar with the diagnostic methods necessary in such cases and with the present-day achievements and relative safety of thoracic surgery. Overestimating the danger of operation and not recognizing the danger of an asymptomatic lesion, they tend to advise their patients to disregard the result of the survey or to submit to occasional follow-up x-ray examinations only. In this way, the chance for early diagnosis and successful treatment offered by the survey detection is lost.

Among the general public more education is needed concerning the rising incidence of bronchogenic cancer. Its detectability in chest x-ray surveys should be emphasized, as well as the possibility of cure if the lesion is discovered early.

Summary

Among 228,375 persons surveyed, 184 (0.8 per 1,000) were considered to have findings suspicious of malignant neoplastic disease.

Twenty-seven cases (roughly 1 per 10,000) of previously unknown primary malignant tumor were found; in 24 of these, the diagnosis was proved by histologic examination.

In the proved cases, 3 patients had Hodgkin's disease, 20 bronchogenic carcinoma and 1 a hemangioendothelial sarcoma.

In the 3 cases of Hodgkin's disease, the diagnosis was established by biopsy of a superficial lymph node; in the 21 pulmonary tumors, the diagnosis was established by surgical exploration in 15 cases, by bronchoscopy in 2 and by demonstration of malignant cells in the pleural fluid in 4.

Sixteen of the patients with pulmonary tumors were subjected to surgical exploration, and 12 were found to have resectable lesions.

Twenty cases of pulmonary metastasis of extrathoracic tumors were found.

In 60 cases, the suspicious x-ray findings were due to nonmalignant conditions; in 16, full-size x-ray film did not reveal any abnormality.

In 58 cases, work-up could not be completed, and the diagnosis remained undetermined.

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TRICHINOSIS WITH NEUROLOGIC AND MENTAL MANIFESTATIONS*

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DESPITE the frequent occurrence of trichinosis in man, its neurologic manifestations have been less commonly recognized. In 1906 Frothingham[1] first demonstrated areas of cellular infiltration containing trichina embryos in the brain of a patient dead of trichinosis. In 1914 van Cott and Lintz[2] first reported the presence of these larvae in the cerebrospinal fluid.

Neurologic manifestations in this disease are often nonspecific, and headache, apathy and drowsiness have frequently been reported. In addition, focal neurologic signs such as loss of deep tendon reflexes,[3] polyneuritis,[4] hemiplegia,[3, 5-7] and both generalized and Jacksonian convulsions[8] have been described. Epileptic seizures have occurred four weeks after onset of the disease[9] and even ten years after recovery.[10] The clinical picture of acute encephalitis has been encountered,[8, 11-13] and 1 case presented the picture of chronic encephalitis with features of a Korsakoff syndrome.[12]

The following cases of trichinosis with neurologic manifestations were observed during a period of two and a half years.

Table 1. *Laboratory and Other Data in 3 Cases of Trichinosis.*

Case No.	Hemoglobin	Hematocrit	White-cell count	Eosinophils	Serologic Test for Syphilis	Non-protein Nitrogen	Blood Culture	Examination of Laked Blood for Trichina	Urinalysis	Spinal Fluid			
										Color	Pressure	Protein	Cells
	gm./100 cc.	%		%		mg./100 cc.					mm. H_2O	mg./100 cc.	per cu. mm.
1	15.0	50	14,450	6-37	Negative (Kahn)	28	Negative (3)	Not done	Negative	Clear	225	18	2 red cells
2	14.6	44	14,850	31-59	Positive (Kahn) Negative (Wassermann)	37	Not done	Not done	Negative	Clear	—	12	3 lymphocytes
3	16.2	51	14,700	25-31	Negative (Kahn)	33	Not done	No larvae found	Negative	Clear	180	35	0

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Case Reports

A 28-year-old machinist was admitted to the hospital on September 29, 1949, because of diarrhea, crampy abdominal pain and vomiting of 11 days' duration. One week later conjunctival hemorrhages and swelling of the eyelids appeared, and 4 days later, on the day of admission, there was stiffness of both temporal muscles. He recalled having eaten pork several times in the preceding month but did not remember whether any of it had been undercooked.

Physical examination showed a well developed and well nourished man, who appeared acutely ill. There was striking periorbital edema, and many subconjunctival hemorrhages. The temporal and masseter muscle groups were tender on palpation. The sensorium was entirely clear, and neurologic examination was negative. The temperature was 101°F., the pulse 112, and the blood pressure 140/94.

Laboratory and other data are summarized in Table 1.

The temperature remained between 101 and 103°F. for the first 2 weeks and then fell to normal. On the 2d day the patient complained of stiffness and soreness of the neck and shoulder muscles. Two days later he became confused regarding time and place and appeared more drowsy. No other abnormal neurologic signs were noted. Some petechial lesions appeared over the chest. Over the next 6 days the confusion cleared progressively, and the subsequent course was uneventful except for several episodes of abdominal cramps. He was discharged well on October 21. When seen 1 month later, he was in good health, but the electrocardiogram still showed ST-segment and T-wave abnormalities, and the white-cell count was 19,800, with 20 per cent eosinophils.

Case 2. A 26-year-old clerk was admitted to the hospital on January 8, 1949, in a confused state. His wife stated that his illness had begun on December 28, 1948, with generalized muscle pains, chilly sensations and severe headaches. He had been admitted to another hospital, where he had received penicillin and a "sulfa drug" without effect. Marked swelling of the eyelids and face, as well as diarrhea, developed and he was then transferred to this hospital. His wife reported that he frequently ate raw frankfurters, bologna and hamburg while at work.

Physical examination showed a well developed and well nourished man, who appeared restless, irritable and confused. He was oriented regarding place but not time. There were no abnormalities of the cranial nerves. Muscle strength could not be tested adequately. The deep tendon reflexes were hyperactive in all extremities, with ankle clonus bilaterally. Superficial abdominal reflexes were present. The plantar reflex was extensor bilaterally, with Hoffmann, Oppenheim and Gordon signs also present bilaterally. No sensory defect was elicited.

The temperature was 99°F., the pulse 90, and the blood pressure 110/70.

Laboratory and other data are summarized in Table 1.

The temperature never rose above 100°F. During the 1st week the patient was somewhat stuporous and required an indwelling catheter because of incontinence. Thereafter his state of consciousness rapidly improved. Three weeks after admission he could walk without difficulty, and neurologic examination revealed no abnormalities. He was discharged well on the 46th day. A blood Kahn test 4 months later was negative. Examination 27 months later again revealed no neurologic abnormalities and a negative blood Kahn test. The previously noted electrocardiographic changes had reverted to normal.

Case 3. A 33-year-old clerk was admitted to the hospital on November 15, 1951, in a poorly responsive condition. His mother stated he had been well until 36 hours before admission, when he had complained of headache and remained in bed. Several hours later he was found lying on the floor unable to move. Subsequent incontinence of urine, but no convulsions, vomiting or diarrhea, was observed. There was no history of recent injury. It was later ascertained that he had eaten "pink" pork chops in a restaurant on October 18 and that swelling of the eyelids had been observed 3 or 4 days before admission.

Physical examination disclosed a well developed and well nourished man, who appeared acutely ill. He was somnolent and responded to questioning only with difficulty. There was a periorbital hematoma on the left. Both eyes deviated to the right. There was slight weakness of the left lower portion of the face. Resistance to passive stretching was increased in all extremities, but more so in the left arm and leg. Muscle strength could not be tested adequately. The deep tendon reflexes were increased, particularly in the left arm and leg. The superficial abdominal reflexes were present and equal. The plantar response was extensor bilaterally. Flexion of the head on the neck resulted in flexion of both thighs. No sensory deficit was elicited.

The temperature was 98.6°F., the pulse 80, and the blood pressure 122/84.

Laboratory and other data are summarized in Table 1.

The patient remained afebrile during his hospital stay. By the 2d hospital day he had become almost completely quadriplegic, the only voluntary motion exhibited being slight flexion of the right leg. At this time he was completely disoriented. On the 4th hospital day ACTH therapy was instituted, 20 mg. being given intravenously over a 24-hour period daily.[14,15] Two days later the patient became responsive, and by the 13th day the rigidity of the extremities had diminished. After 17 days of therapy, the ACTH was discontinued because of the appearance of occult blood in the feces. By this time he was able to move his right arm and hand and to flex the right leg, but motion on the left was minimal. All attempts at motion were accompanied by grimacing expressions and by whistling through the teeth. Over the next 2 weeks his strength was such that he was up in a chair, and by the 5th hospital week he was able to walk without assistance. At the time of discharge from the hospital, he still had residual weakness of the muscles of the left arm, and 1 month later (5 months after onset), evidence of bilateral corticospinal-tract damage was still present, although less marked than previously.

Table 1 (*Concluded*).

Case	Spinal Fluid			Chest X-Ray Examination	Electrocardiogram	Electroencephalogram	Skin Test for Trichina	Muscle Biopsy	Complement Fixation	Other Complement-Fixation Tests*
	Colloidal-gold test	Wassermann test	Culture							
1	Negative	Negative	Not done	Negative	ST-segment and T-wave changes	Not done	Positive	Positive	Not done	Not done
2	Negative	Negative	Not done	Negative	ST-segment and T-wave changes	Not done	Positive	Negative	Positive	Not done
3	Negative	Negative	No growth	Negative	ST-segment changes	Paroxysmal 5-6 per second wave bilaterally	Negative → positive	Positive	Negative → positive	Negative

Discussion

The cycle of *Trichinella spiralis* in human beings begins with the ingestion of trichinous pork that has been insufficiently cooked. The cyst surrounding the embryo is digested, and the parasite attaches itself to the wall of the small intestine. Here, after maturation and copulation, the female deposits motile larvae, which enter the intestinal lymphatic vessels and, via the thoracic duct, the venous blood stream. The larvae then pass through the lungs into the systemic circulation. Distribution of the larvae may be universal, but it is only in striated muscle that they leave the blood capillaries to penetrate the sarcolemmal sheaths and encyst. Clinical and pathologic changes result either from passage through or lodgment in the affected areas.

The gross pathologic changes in the nervous system consist for the most part of an acute nonsuppurative meningoencephalitis.[8, 12, 16, 17] Microscopically, there is perivascular infiltration and endothelial proliferation, plugging with fibrinous thrombi and rupture of the small-blood-vessel walls. In addition, granulomatous nodules surrounding free young trichinae have been described. Finally, degenerative changes such as chromatolysis with fatty degeneration of ganglion and glial cells may be seen. All these changes are most common in the subcortical white matter of the brain.

In addition to the usual signs and symptoms of trichinosis, such as fever, gastrointestinal disturbances, periorbital edema and muscle tenderness, the patient in Case 1 demonstrated confusion, drowsiness and disorientation, suggesting interference with higher levels of cortical function. In Case 2 there were signs of more extensive nervous-system involvement — namely, hyperreflexia, ankle clonus and extensor plantar responses, in addition to restlessness, irritability and confusion. These abnormalities were transient, however. The patient in Case 3 had the most severe nervous-system involvement, manifested by an acute meningoencephalitis. The almost complete quadriplegia gradually improved, although examination five months after onset revealed some neurologic deficits. It is of interest that this patient did not exhibit gastrointestinal symptoms, muscle tenderness or fever at any time during his hospitalization.[7] The improvement in his condition noted two days after the administration of ACTH was begun could not be attributed to this therapy with certainty. All 3 patients showed cardiac involvement (myocardial or pericardial), as evidenced by ST-segment and T-wave abnormalities in the electrocardiograms. In Case 3 these changes were still present five months after onset of the illness.

Summary and Conclusions

Three cases of trichinosis with varying degrees of central-nervous-system involvement are presented, and the neuropathological features of this disease are briefly reviewed.

Severe neurologic defects may occur with but few of the usual symptoms and signs of trichinosis, thereby presenting a problem in diagnosis.

All 3 patients showed electrocardiographic abnormalities.

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MEDICAL PROGRESS

OCCUPATIONAL MEDICINE (Concluded)

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Apparently Benign Pneumoconiosis

The inhalation of certain dusts may produce x-ray pictures that are alarming in appearance. However, there is no reaction to such dusts and their chief hazard is mistaken diagnosis, with resultant unnecessary anxiety and poor medical advice to the worker. Hamlin[117] has recently discussed the differential diagnosis between silicosis and siderosis, the benign x-ray picture caused by inhalation of iron oxide. The term benign pneumoconiosis is applied to these cases, and the physician will do well to acquaint himself with the available facts. Hamlin and Weber[118] have made clinical and chest x-ray studies of 69 foundry grinders and burners exposed to iron oxide dust containing small amounts of free silica. They discuss in detail the nodular shadows seen in the x-ray films of 9 of these workers to bring out the differential diagnostic points among the iron-dust shadows, siderosis and the disease-producing densities of silicosis. The air analysis showed exposures of these men to be between 14 and 224 mg. of iron oxide per cubic meter of air and less than the safe level of 5,000,000 particles of free silica per cubic foot of air. Vorwald and associates follow this clinic report with an experimental study of siderosis in which they found round or elongated foci of radio-opaque iron oxide in the exposed rabbits' lungs without fibrotic reaction. The same was true in guinea pigs, which also showed no change in tuberculous infection because of the inhaled iron oxide. Even though the foundry dust contained 4 per cent of crystalline free silica, Vorwald et al.[114] believe that this foundry dust should be characterized as "inert." Sander,[119] discussing siderosis says that in following a group of electric welders with siderosis for twenty years he has seen no disturbance in lung function and no increase in incidence of pulmonary cancer. He cites Doig and McLaughlin[120] as finding clearing of the chest x-ray shadow in a similar group of workers with siderosis but says that this has not been his experience. Tin oxide inhalation has also been reported as producing a characteristic x-ray picture. Dundon and Hughes[121] have presented such a case in which the history showed that the patient had tended a detinning furnace, which recovered tin scrap by a calcining process, for eighteen years. Barták and Tomecka[122] report stannosis found incidentally in the lung of a forty-nine-year-old man who died of cancer of the stomach. Tin was demonstrated in the lungs, liver and spleen. Out of 16 workers similarly exposed, x-ray evidence of stannosis was found in 6. These workers were exposed to the dust and fumes from a furnace in which pure tin was burned to tin oxide.

Miscellaneous Occupational Diseases of the Respiratory Tract

Stephanopoli de Comnène and Besson[123] report that out of 84 dock workers at the port of Marseilles 21 had pneumoconiosis. They consider this a true disability caused by the inhalation of cereal dusts contaminated with appreciable amounts of silica and believe that if the workers are not removed from exposure to the cereal dusts "in the first stage of chronic bronchitis and dyspnea" they will progress to a status of complete disability.

Schilling,[124] working in England, has made complete studies of cotton-mill workers and presented his findings. He characterizes byssinosis as chronic interstitial pneumonia due to cotton dust. Schilling and also Emerson,[125] presenting a case and reviewing the literature, point out that byssinosis may early appear to be only an asthma-like reaction, but without relief from exposure the process may progress to irreversible pulmonary fibrosis, with emphysema and consequent cor pulmonale. Ideas of etiology include allergic reaction to bacteria, fungi or molds. Furness and Maitland[126] have recently made extensive studies of cotton dust, searching for both variation in physical character and bacterial and fungal content among cotton of different grades and origins. They found nothing they considered relevant. Purely mechanical irritation and foreign-protein reaction have been held responsible for byssinosis. Emerson points out that cotton dust contains histamine.

Schilling and Goodman[127] have investigated the Registrar General's figures showing high death rates from cardiovascular diseases among cotton workers. They find the excess cardiovascular mortality sometimes assigned to inhalation of cotton dust to be real and especially high among strippers and grinders. Further studies have just been presented by Schilling, Goodman and O'Sullivan[128] (April, 1952), after these authors had made a clinical study of cotton-mill workers. They report a real increase in hypertension among the 63 per cent of card and blow-room workers who had symptoms

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of byssinosis. The authors believe that there is a suggested relation "between industrial respiratory disease and hypertension" that they plan to study further. Proudfit, Van Ordstrand and Miller[129] have reported in detail a case of chronic lipid pneumonia following exposure to a spray of "mineral oil" used in lubrication of cash registers. The patient, forty years of age at the time of the report, had been engaged in the servicing of cash registers for seventeen years. The man complained of cough and dyspnea, and x-ray examination showed changes similar to those seen after lipiodol injection. Oil globules were demonstrated in the sputum.

TABLE 1. *Summary of Major Toxications of Insecticides Interpreted in Terms of Human Toxicology.**

COMPOUND	LOCAL EFFECT	PREDOMINANT SYMPTOMS	ESTIMATED FATAL DOSE	PERIOD BETWEEN EXPOSURE AND DEATH	TREATMENT
			gm.		
Rotenone	Irritation	Stupor, frequent convulsions, respiratory depression and death	200.0	2–3 days	General and symptomatic
Pyrethrins	None	Inco-ordination, tremors, muscular and respiratory paralysis, and death	100.0	3–5 days	General and symptomatic
Nicotine	Irritation	Tremors, convulsions, curare-like paralysis and death	0.060	Minutes	General artificial respiration
Lethanes	Irritation	Deep depression, cyanosis, dyspnea, tonic convulsions, respiratory paralysis and death	(28–70 of concentrates)	Within 12 hr.	General and symptomatic
DDT	None	Giddiness, nervous tension, involuntary muscular tremors, convulsions, depression, respiratory failure and death	30.0	2–24 hr.	General (phenobarbital)
Methoxychlor	Slight irritation	Questionable tremors and depression	450.0	2–4 days	General and symptomatic
TDE	Slight irritation	Lethargy	300.0	1–4 days	—
Chlordane	Irritation	Convulsions, depression repeated several times, deep depression and death	5.0–60.0	1–4 days	General and symptomatic
Toxaphene	Irritation	Epileptiform convulsions and death	7.0	4–24 hr.	General (phenobarbital)
Benzene hexachloride	Irritation	Hyperirritability to outside stimulus, occasional convulsions, depression and death	30.0	1–5 days	General and symptomatic
Organic phosphates (TEPP—Parathion)	Irritation	Lacrimation, salivation, sweating, nausea, vomiting, diarrhea, respiratory distress, disturbance of vision, headache, muscular tremors, generalized collapse and death	0.012	1–4 hr.	General and symptomatic; atropine; magnesium sulfate.

*Based on Lehman.[131]

TOXIC CHEMICALS

Pesticides

Development in the field of chemicals for destruction of all varieties of pests bothersome or dangerous to human beings, animals or vegetation has expanded greatly in recent years. The Council on Pharmacy and Chemistry of the American Medical Association has appointed the Committee on Pesticides, which presents reports for publication as deemed advisable. The 1951 report on benzene hexachloride[130] effects is an excellent example. Table 1 is offered to help the physician judge the seriousness of a case of poisoning after exposure of a householder or an agricultural worker to one of the many insecticides in current use.

The organic phosphate insecticides[117]—commercial examples are known as TEPP and Parathion—act to reduce the blood cholinesterase level, with resultant stimulation of the parasympathetic nervous system.[132] By measuring the red-cell and plasma cholinesterase levels of exposed workers, Brown and Bush[133] conclude that air concentrations of 2 to 8 mg. per 10 cubic meters of air may be dangerous. Barnes and Davies[134] examined 80 exposed workers and found 12 with depressed blood cholinesterase activity. Callaway, Davies and Rutland,[135] by studying the range in variation of such levels, further show blood cholinesterase levels to be a useful means of medical control. A series of articles published by the American Medical Association in 1950 by a group of authors[136] sets forth the available knowledge of industry, state authorities and research workers of the dangers of organic phosphates used as insecticides. In this report, Abrams describes in detail 8 cases of intoxication and says that in the country as a whole there have been 112 cases in agricultural workers, 56 in industrial workers and 4 in children exposed to organic phosphates. Disturbance in vision caused by these chemicals has resulted in accidents when pilots have been engaged in spraying crops. Ingram[137] describes cases of illness of pilots in this work and the problems associated with the control of this hazard. Since the material can penetrate the unbroken skin, there have been cases of illness and death because of ignorance of need for protection. Atropine is specific and life saving, as the case reports show, if administered in time. Williams and Griffiths[138] present 5 cases of Parathion poisoning in citrus-spray operations and report that in 4 of these the symptoms

of poisoning appeared when the red-cell cholinesterase was between 50 and 75 per cent of the normal control. This, they conclude, means that there may be warning symptoms before the dangerous level of 25 per cent is reached.

Aldrin is a new insecticide for the control of boll weevils. *Life Magazine* for June 30, 1952, shows American workers using it as a spray from a plane to control a plague of locusts in Iran. Spiotta reports[139] a case of poisoning, a suicide attempt, demonstrating that Aldrin produces a cerebral dysrhythmia causing convulsions hard to control and hematuria and albuminuria indicating renal damage. Small-animal studies showed degeneration of the renal tubules, hepatic necrosis and ganglion-cell degeneration.

Bidstrup and Payne[140] report 7 fatal cases among men using dinitro-orthocresol (DOC) as a selective weed killer in British cereal crops, and the death of 1 working on manufacturing the material. Death takes place quickly after unusual sweating, thirst and abrupt weight loss, symptoms that usually, in hot weather, appear to be heat stroke. Pollard and Filbee[141] report recovery in a case of DOC poisoning of a worker who failed to put on a face mask while spraying. They report a high basal metabolic rate, high nitrogen excretion and high blood urea levels. Animal studies by Parker, Barnes and Denz lead them to postulate that DOC acts to inhibit the formation of adenosine phosphate. This means that the energy formed by body oxidation cannot be converted to a useful form and so is dissipated as heat.

Air Pollution

Because of abnormal weather conditions an unusual condition of atmospheric pollution occurred in a Pennsylvania industrial town in 1948, resulting in deaths in the community. This episode, known as the Donora Smog, was reported by Shrenk and his associates[142] after a careful study for the United States Public Health Service. It was concluded that a combination of chemicals was probably responsible for the morbidity and mortality. Los Angeles, owing to its expanding industry and physical location, has complex air-contamination problems. This is well discussed by Baetjer in the 1951 edition of *Roseman's Preventive Medicine*.[143] The matter is mentioned here since physicians will be concerned in the question of true cause and effect in industrial communities where atmospheric pollution is certain to occur. Committees representing all skills and interests have been set up for study, and restrictive legislation has been proposed. The control of radioactive-waste contamination in neighborhood air is carefully supervised by the Atomic Energy Commission.

Ten cases of chronic beryllium poisoning due to relatively slight exposure, as measured, of persons living near certain beryllium industries have been reported by Chesner[144] from Ohio, supplementing earlier reports of neighborhood cases. This specific problem of air pollution has been handled, by 1 plant by discontinuation of the use of beryllium and, by another, through moving to a site at a reasonable distance from dwellings.

Beryllium Poisoning

Dr. Alice Hamilton remarks that the speed and thoroughness with which the problem of illness among workers exposed to certain beryllium compounds has been studied and largely controlled is in her experience remarkable. Study of the literature since Tabershaw[145] wrote a report for this journal in 1949 bears out this observation. Sterner and Eisenbud,[146] discussing the epidemiology of beryllium poisoning in 1951, point out the neighborhood contamination and many incriminated operations, all of them involving exposure to beryllium oxide. Aub and Grier[147] presented a report of acute beryllium pneumonitis in workers exposed to beryllium metal and the oxide. Previous records of acute beryllium pneumonia have followed work exposure to soluble beryllium compounds. Cases of acute beryllium poisoning are now rare when the toxicity of beryllium is understood and handled by proper engineering measures and medical control. However, chronic cases still appear, in part because of the delay in onset between cessation of beryllium and onset of disease. Sterner and Eisenbud[146] suggest that a chronic allergic reaction could account for the production of the granulomatous response of chronic beryllium poisoning after a long latent period. They believe that an immunotoxic reaction may explain the small amount of beryllium compound that apparently causes disease in some cases and the response of other organs in producing the systemic manifestations of chronic beryllium poisoning.

Diagnosis of chronic beryllium poisoning has been aided by an increase in the availability and knowledge of changes in pulmonary-function studies. Bruce and his co-workers[148] have reported their findings in a series of 10 cases of chronic beryllium poisoning. Wright,[149] Ferris[150] and McClement[150] have discussed the same subject. These authors agree that chronic beryllium poisoning produces a pathologic process that interferes with the passage of oxygen across the alveolar membrane, with resultant lowered arterial oxygen saturation. As the disease progresses, emphysema is demonstrated in varying degree. Clinical experience* shows a marked discrepancy among the chest x-ray changes, the disturbance in lung function and the patient's clinical status.

On occasion the diagnosis of chronic beryllium poisoning may be difficult because of the inability to get a complete and accurate exposure history owing to change in industrial operation or long-discontinued neighborhood contamination. Assay

*Unpublished data of the Occupational Medical Clinic, Massachusetts General Hospital.

of urine for the presence of beryllium can be carried out in properly equipped laboratories. Klemperer, Martin and Van Riper[151] have studied this problem. They found no beryllium in 35 controls with no beryllium exposure. They found that healthy workers exposed to soluble beryllium salts had the highest excretion levels. On the other hand, only 12 of 20 patients with chronic beryllium poisoning excreted detectable beryllium. Of those who excreted beryllium, the daily excretion was at a constant level during the period of study. Beryllium was found in the urine of an exposed worker as long as ten years after cessation of beryllium inhalation. Klemperer et al. speculate that a physicochemical interaction of the surface of a solid insoluble beryllium particle with tissue elements may be the cause of the pathology of beryllium disease. It follows from this work that beryllium in urine establishes exposure but does not make a diagnosis of intoxication and, conversely, absence of beryllium in urine does not dispute a diagnosis of chronic beryllium poisoning.

Clinical description of chronic beryllium disease has recently been supplied by a collection of papers presented at a meeting held in December, 1950, to discuss the usefulness of ACTH and cortisone in chronic beryllium poisoning.[150] These reports suggest that the steroids do change at least temporarily disturbed biochemical and pulmonary-function values, indicating objectively that there has been a response. In a few cases evidence of improvement in chest x-ray changes was presented. No toxic effects were reported. Dobson and Weaver[152] have reported a case of chronic beryllium poisoning complicated by pulmonary tuberculosis. By use of ACTH when the patient seemed in terminal clinical status his life was prolonged at an improved level for some months. White, Finkel and Schubert[153] have suggested that aurin tricarboxylic acid, a laking agent, be used in the treatment of chronic beryllium poisoning. They believe that beryllium cannot be made to leave the body and that, if it can be surrounded and fixed when it lies in tissue, its toxic effects may be annulled. They have had marked success in small animals with acute beryllium poisoning. Studies are in progress to determine the toxicity of aurin tricarboxylic acid and its usefulness in animals chronically exposed to beryllium compounds. Finkel and White[154] have shown that the salicylates chemically related to aurin tricarboxylic acid have a similar effect experimentally because of chelation effect.

The reactions of skin to certain beryllium compounds have been a source of interest. Helwig[155] reports 10 cases of chemical granulomas of the skin and reviews critically the data on the subject available to 1951. He believes that there is a biphasic reaction, consisting of granulomas of epithelioid cells and necrobiosis composed of acidophilic anuclear tissue, that results in ulceration. He postulates that beryllium acts with other elements to produce this result. Curtis[156] has studied the dermatitis seen in workers exposed to soluble beryllium salts that, he believes, is an allergic eczematous reaction. He says that beryllium is insoluble with respect to skin and sweat. Anions, acidity and primary irritation of soluble beryllium compounds are eliminated by Curtis as direct causative factors. He holds that beryllium acts as a sensitizing allergen and suggests that the mucous-membrane reactions, including the acute pneumonitis following exposure to certain soluble beryllium compounds, may be allergic reactions. McCord[157] has verified this skin reaction with personal experience.

MacMahon and Olken[158] have presented in detail the case records and post-mortem findings of 2 workers with chronic beryllium poisoning exposed to beryllium phosphors in fluorescent-lamp manufacturing. They point out that the extent of damage to alveoli, atria, alveolar ducts, bronchioles, blood vessels and lymphatics is adequate to explain the clinical picture.

A great deal of animal work has been done with certain beryllium compounds in the past few years, but only a few of the studies that appear relevant to the problem of the disease in human beings are discussed in this paper. No cancers have appeared as yet in worker cases of beryllium disease, but confirmatory production of sarcomas in rabbits is reported by Barnes et al.[159] Hoagland and his associates[160] and Nash,[161] as well as Dutra and Largent,[162] produced such tumors by inhalation of beryllium oxide, whereas all other workers have used the intravenous route. Dutra[163] also produced granulomas by introducing beryllium compounds under the skin of pigs. This is the first commonly accepted chronic tissue response produced in the United States. Policard[164] and Davies and Harding[165] have presented evidence of granulomas produced in lungs of small animals with certain beryllium compounds. The observations of Grier et al.,[166] confirmed and extended by Klemperer[167] and by DuBois and his co-workers,[168] that beryllium inhibits alkaline phosphatase enzymes may have some bearing on the mechanism of beryllium toxicity in biologic tissue.

Stokinger and his associates[169-172] have presented satisfactory animal evidence that beryllium is the cause of acute beryllium poisoning and does not require the acid radical for the action. Aldridge et al.[173] have reported acute beryllium poisoning in small animals as causing considerable hepatic necrosis. Schubert and White,[174] in trying to shift and excrete beryllium from the body by using citrate salts, believe their studies indicate that the toxicity of beryllium salts is due to ionized beryllium.

Lead Poisoning

Kehoe[175] recently stated that blood lead assay is the "most important single bit of evidence required to portray the significance of the absorption of lead" in a given patient supposed to suffer from

lead intoxication. He urges duplicate samples that check to be certain of a given blood lead value.

Other workers have concentrated on the value of qualitative and quantitative urinary coproporphyrins as an index of lead intoxication. Waldman and Seideman,[176] using the semi-quantitative test, found no false-negative reactions in 116 men exposed to lead, and in all urines with more than 0.15 mg. of lead per liter positive tests were obtained. Maloof,[177] after study of several hundred urine samples, says that although quantitative urinary coproporphyrin studies are not specific for lead poisoning, they are consistently high after hazardous exposure. This author finds that coproporphyrinuria occurs earlier than an increase in stippled red blood cells in lead intoxication. McCord[178] has reviewed the literature and concludes that porphyrinuria is absent from healthy workers and when present in lead workers may be regarded as of diagnostic importance. Brooks, after doing 952 porphyrin in urine tests, qualitative in character, on 92 workers under his care reaches the same conclusion. Dart, after 245 simultaneous tests for porphyrin in urine and basophilic aggregation counts, believes that a close correlation exists.

Grinstein et al.,[179] working with radioactive glycine in lead-poisoned rabbits, show that urinary coproporphyrin III is not related to hemoglobin catabolism as has been suggested but is newly formed as a result of the toxic effect of lead.

Hay[180] has presented an interesting report of lead encephalopathy in 1 of 4 men engaged in the repair of wooden barrels that had contained white lead. Air lead analysis showed concentrations of from 50 to 1300 mg. of lead per 10 cubic meters (the safe concentration is considered to be 2 mg. per 10 cubic meters). Repeated lumbar puncture was considered life saving.

Berger and Lundberg[181] have reported intestinal volvulus after acute plumbism in 5 cases. The volvulus involved the sigmoid and the small bowel and required operation.

In spite of the fact that removal from lead exposure is the treatment most certain of success, reports of new forms of therapy continue to appear. British Anti-Lewisite (Dithiopropanol) has not proved as useful a treatment for lead intoxication as might have been expected after the success achieved in other metal poisonings, notably acute mercury and arsenic poisoning. Stocken and Thompson,[182] in a recent review article, say that BAL may increase lead excretion temporarily, but there is no evidence that intoxication is cured. Anderson,[183] studying lead poisoning in mice, concludes that BAL is of no value. Bastrup-Madsen[184] presents 2 interesting cases of women who were acutely poisoned by lead taken as oral litharge to induce abortion. In a short follow-up study, he showed marked increase in lead excretion but reported no change in symptons after using BAL.

Zeglio,[185] discussing the use of BAL in industrial diseases in Italy, reports that experimental work with animals indicates that the material is harmful. In human cases Zeglio says that the blood lead was reduced by BAL administration but rose when the drug was stopped. Vigliani and Zurlo[186] have described their experience using BAL in industrial lead poisoning in 27 patients after studies of blood and urinary levels. They conclude that BAL is a dangerous form of therapy in lead poisoning. They point out that the action of BAL is to move the lead within the body from blood and other tissues, and by this action greater damage may be caused, especially if the lead is transported to the nervous system. The general effect of the work presented to date justifies the conclusion that BAL is not a good form of therapy in lead poisoning.

Proctor and Kahn[187] advocate the use of disodium hydrogen phosphate in lead poisoning because of its action in producing the insoluble $Pb_3(PO^4)_2$ that is excreted. They report favorably on 8 cases.

Shiels, Thomas and Palmer[188, 189] urge that there are good grounds for using sodium citrate as treatment and as preventive therapy for lead poisoning. They gave 48 lead workers in a storage-battery plant 4 gm. of sodium citrate daily and showed by stippled-cell counts that the drug was of definite value. Fortunately, they point out that the sodium citrate is not a substitute for adequate engineering protection. Hardy, Bishop and Maloof[190] reported in detail on 4 cases of lead poisoning treated with sodium citrate. They found that in high enough doses sodium citrate will control the symptoms. However, careful studies of urinary excretion showed no significant and regular increase in lead excretion, contrary to previous claims.

There is some evidence that a chelating agent, ethylene diamine tetra-acetic acid, as a calcium salt will complex with lead and prove of great merit in human lead poisoning.[191] Its use is in the experimental stage, but reports in 1 childhood[192] and 4 adult cases[193] of lead poisoning are promising.

Schubert and White[174] suggest that zirconium citrate may increase lead excretion to a remarkable extent without affecting blood lead. Their work was done on small animals with radioactive lead. These authors say that their studies show that sodium citrate is without effect on blood disappearance rate, tissue distribution or excretion of lead. Schubert and White urge that zirconium citrate, which they say is harmless, be tried in cases of lead poisoning in human beings.

Miscellaneous Toxic Chemicals

There are two interesting reports of occupational mercury poisoning in recent years. Agate and Buckell[194] describe the cases of 7 policemen using a mercury-containing powder for detecting latent fingerprints who showed classic signs and symptoms of poisoning. The authors describe tremors, psychic irritability, loosening of the teeth and abnormally

high urinary mercury levels. Bidstrup et al.[195] report that 27 of 161 direct-current meter repair men examined showed chronic mercurialism. This article, which appeared in the *Lancet*, was accompanied by an editorial commenting on the fact that one of the workmen had read of the symptoms of mercury poisoning, recognized them as his own and went to his physician, who had been puzzled by the man's illness. The workman could report that he and his affected fellow workers were exposed to as much as 8 pounds of metallic mercury daily.

Hematologic studies of mercury workers have been reported. Goldwater,[196] examining men in the fur-felt-hat industry, found elevated hemoglobin levels and macrocytosis. Kesic and Haeusler,[197] in complete blood studies of 130 mercury miners, 59 mercury-smelting-plant workers and 70 women workers in a felt-hat factory, could find no significant alteration in hemograms.

Review articles such as that of Stocken and Thompson[182] continue to affirm the success of BAL in the treatment of acute mercury poisoning. There is no evidence of the place of this drug in chronic mercurialism.

Arsine formed when an acid solution attacks any arsenic-containing material, as recently discussed by Morse and Setterlind,[198] is a constant source of occupational hazard because it is an intense and rapid hemolytic poison. Spolyar and Harger[199] discuss the epidemiology of an industrial accident that exposed 21 men to arsine with hospitalization necessary for 13 men and a fatal outcome in 4 cases. The exposure arose when moisture reacted with aluminum arsenide during purification of lead alloys. Pinto et al.[200] reported on the clinical picture that developed five hours after exposure beginning as nausea, vomiting, abdominal cramps and hemoglobinuria. There was initial leukocytosis — white-cell counts of 13,000 to 29,000. Electrocardiograms showed distinctive changes, which Josephson, Pinto and Petronella[201] discussed in detail. The 4 deaths from arsine were due to myocardial failure. BAL did not prevent or stop the hemolytic process, and repeated blood transfusions were shown to be the treatment of choice.

Reports of cadmium intoxication are rare. Cotter and Cotter[202] discuss the cases of 5 men exposed to varying amounts of several different cadmium compounds. They conclude that since cadmium was found in blood and urine, certain transient laboratory values of liver, kidney and bone-marrow function indicated that these men suffered cadmium intoxication.

Friberg[203] has reported the findings in a study of 43 men exposed to cadmium and nickel dust in an alkali-storage-battery plant. These included emphysema of the lungs evaluated by spirometry, proteinuria in 35 to 43 men, increased red-cell sedimentation time and change in renal function as measured by inulin clearance or maximum concentration ability. The average length of exposure was twenty years. Many of these findings were reproduced in animals. This is Swedish experience, and there are as yet no reports of such a clinical syndrome in American workers exposed to cadmium or cadmium and nickel dust. Variation in the character of the exposure may account for this. Princi and Geever,[204] studying the prolonged inhalation of cadmium in dogs, did not find significant pulmonary or renal changes. Friberg,[205] on the other hand, working with radioactive cadmium in animals, showed the proteinuria that he has reported in human beings exposed to cadmium.

Potts et al.,[206] working with radioactive cadmium in animals, find that an inhaled cadmium compound is highly concentrated in lungs and liver, and an injected compound is concentrated in the liver and kidneys.

Vanadium encountered in the petroleum industry in this country has been the subject of a monograph by Sjöberg.[207] He concluded, after clinical observation and animal study, that earlier industrial reports of acute respiratory irritation, occasionally including pneumonia, are justified.

Williams[208] reports 8 cases of vanadium poisoning in men engaged in cleaning oil-fired boilers. They complained of sneezing, coughing, sore throat and tightness of the chest. In all cases the tongue was covered with a yellowish-green coating. In 4 cases rales and rhonchi over both lungs were heard. With relief from exposure these symptoms disappeared. BAL has no therapeutic effect on acute vanadium poisoning in small-animal experiments, as reported by Lusky, Braun and Lang.[209]

Roberts[210] describes platinosis as a mild chemical irritation of the skin producing chronic inflammation of the entire respiratory tract "including an apparently harmless pulmonary fibrosis." Platinosis occurs in platinum refining after exposure to soluble platinum salts. A case of manganese poisoning occurring in a worker after two months of breaking up and loading manganese ore is reported by Ceresa.[211] The patient had a dermatitis, bronchitis and an enlarged liver cured by BAL therapy. Davies and Harding,[212] after clinical and experimental studies, have shown that manganese dust will produce a specific pneumonitis. They incriminate the high oxides and the dioxide of manganese.

Harding,[213] after animal study, finds that cobalt metal causes acute capillary damage, which is related to the solubility of the cobalt in protein-containing fluids. His animals showed severe pulmonary edema and hemorrhage when exposed to cobalt-metal powder. Harding and Davies[214] demonstrate that inhalation of zircon (zirconium silicate) produces dense shadows on an x-ray film of the rat's lungs. They find these densities to be due to phagocytes containing zircon, with no reaction. They

suggest that since zircon appears so inert it might be used as a substitute for silica when possible.

In animal experiments with rabbits and rats, Barnes and Denz[215] could show no protection by BAL against nickel carbonyl poisoning unless the drug was given prophylactically.

Nilsby[216] reports 7 cases of chronic benzene poisoning among shoe workers using various cements. Benzene was substituted for the harmless benzoline during the war. All the patients died in spite of early treatment with liver, folic acid, iron and multiple transfusions. Nilsby points out that the evidence of benzene poisoning appears from months to years after exposure has ceased.

Blaney[217] discusses his plan to prevent benzene effect or detect it early should it occur in the 75 to 90 exposed men whom he was studying in a plant making polyvinyl plastics. He describes the changes in the hemograms of 2 workers that prompted him to shift their jobs. One man showed a gradual downward trend in blood levels, and the other an eosinophilia. Both men had normal counts eventually.

Galavotti and Troisi[218] present an interesting case of what they term erythroleukemic myelosis resulting in the death of a chemical worker. This man was exposed to benzene in the manufacture of hexachloro-cyclohexane. Fellow workers showed changes in their hemograms. The authors discuss the available evidence that benzene produces leukemia-like pictures in animals and in human beings.

Hardy[219] raises the question whether more than one occupational or iatrogenic factor may combine to produce fatal blood dyscrasias. Two cases are presented, the first being that of a man exposed to trinitrotoluene and later benzene; the second was assumed to have been exposed to benzene and later to ethylene dichloride.

Bousser et al.[220] report the case of a man who applied a benzene-containing paint for two years and after a delay of three and a half years without exposure developed a blood dyscrasia. At autopsy lymphosarcoma was found. Benzene was detected in the spleen and lymph nodes. The authors speculate that this malignant lesion was caused by benzene.

There are still many reports of carbon tetrachloride poisoning appearing in the current literature. Prag[221] reports the case of a man who had cleaned electric equipment with the material. His death was considered to be due to hemorrhagic pulmonary edema. Smith[222] reported 3 cases of optic atrophy due to carbon tetrachloride, only 1 case showing systemic intoxication. Norwood[223] presents his experience with carbon tetrachloride poisoning, which includes 3 severe cases, 4 mild cases and 51 exposures from improper working conditions. He urges national labeling regulations. Friedberg[224] reports 4 cases of carbon tetrachloride poisoning, emphasizing the fact that retention of sodium and water due to the toxic renal disease presents a picture of often confusing congestive heart failure. He urges care in giving fluids and illustrates his points with the clinical histories. This author, as do Norwood and McGee[225] in presenting 3 cases, points out the frequent synergistic action of carbon tetrachloride with alcohol. In the cases of Norwood and McGee 2 men, 1 cleaning a floor and 1 using the chemical to put out a fire, had both been drinking, as had 1 woman who was cleaning furniture in a trailer. These authors emphasize the renal involvement as crucial in plans for treatment. Moon[226] describes the pathology of carbon tetrachloride poisoning in 12 patients, 11 of whom gave a history of considerable intake of alcohol. Moon finds no difference in the lesions produced by inhalation and ingestion. In early deaths the hepatic damage is prominent; in those who survive longer, varying degrees of renal disease and pulmonary edema are seen.

Sirota[227] has done careful studies of the mechanism of renal failure and recovery in carbon tetrachloride intoxication. Koch-Wesser et al.[228] can show protection of rats' livers against carbon tetrachloride if large enough doses of vitamin B_{12} are given prophylactically. Their studies demonstrate that carbon tetrachloride probably acts as a vasodilator and not primarily on nucleic acid.

Miscellaneous single reports of toxic occupational accidents are grouped together for convenience. Troisi[229] states that 9 out of 38 women suffered loss of consciousness, and 14 women showed nystagmus after exposure to ethylene glycol in an electrolytic-condenser factory. Removal from exposure resulted in complete cure. LeWinn[230] describes the case of a research chemist who inhaled diazomethane gas. He died a hundred hours after exposure, with cerebral symptoms, albuminuria and relative hypertension. Autopsy showed toxic changes in the heart, kidney and liver, as well as inflammatory reaction in the lungs and gastrointestinal tract and areas of necrosis in the brain.

An interesting study to evaluate safe occupational exposures to methanol has been made by Leaf and Zatman.[231] Using human volunteers they find 300 parts per 1,000,000 parts of air a safe working level. They say that ethanol ingested with methanol reduces the rate of elimination up to 90 per cent because of inhibition of metabolic oxidation of methanol. This, they believe, accounts for the favorable action of ethanol ingestion in methanol poisoning.

Baader and Bauer[232] report occupational illness due to exposure to pentachlorophenol, which is being developed as an insecticide and fungicide. They report 10 cases showing a serious acne and pain along the peripheral nerves, in addition to irritation of the respiratory tract. The clinical findings are similar to those reported from intoxication due to chlorinated naphthalenes.

A review of the literature on ozone toxicity has been presented by Thorp.[233] He shows that early reports of toxicity of ozone were in error because of contamination of the ozone in air with nitrogen oxides known to be pulmonary irritants.

Larner[234] has written a similar review article of the toxic behavior of occupationally encountered fluorine-containing compounds. There are many articles on this subject and few reports of illness in industry incriminating fluorine compounds.

Vigliani[235] presented his clinical observations in 100 cases of carbon disulfide intoxication occurring in plants manufacturing synthetic textile fibers. The clinical pictures included polyneuritis, gastric disturbance, headache and vertigo, sexual disturbance, tremors, psychoses and optic neuritis in that order of occurrence.

Ethylene amines have only recently been produced in quantity. Dernehl[236] reports 14 cases of reaction to these chemicals and concludes that both irritation and allergy are responsible for the skin and respiratory-tract symptoms he describes.

Figley and Rawling[237] studied 9 cases of castor-bean allergy causing asthma in workers exposed to the dust from burlap bags. The authors did an interesting detection job since these bags were used by their patients for shipping green coffee and metal castings but had previously been used for shipping material contaminated with castor pomace. The authors also learned that green coffee may be contaminated with a castor-bean derivative. On freedom from exposure their worker-patients had complete relief of symptoms.

Zucker et al.[238] reported a case of pulmonary involvement after aspiration of gasoline. They believe that the right-lower-lobe pneumonia that occurs is due to gasoline aspirated directly into the trachea and not, as suggested, to vapors excreted from the pulmonary circulation.

Ingram[239] reported on the hazards of methyl bromide exposure in the date-packing industry. The methyl bromide used as a fumigant produced about 200 cases of worker illness in the California industry. He observed symptoms related to the gastrointestinal tract and to the nervous system, resulting in reactions varying from loss of balance to alcoholic-like states and, in acute cases, to psychotic episodes requiring hospitalization. Methyl bromide is also used in fire extinguishers and has been employed as a refrigerant, producing accidental poisoning and death as reported by Prain and Smith.[240] These authors describe 8 cases in schoolboys, exposed in a prank, with renal and central-nervous-system abnormalities.

Wolfsie[241] has given a clear and helpful account of what may be life-saving steps to be taken in cases of cyanide poisoning, which can occur under the best of conditions. He reports in detail the safe handling of 11 cases. Treatment is based on the knowledge that sodium nitrite will form cyanomethemoglobin, which will then, by administration of sodium thiosulfate, form thiocyanate, which the body can handle safely.

Spolyar et al.[242] have reported the generation of phosgene in a trichloroethylene degreaser that was prepared for perchloroethylene. The phosgene was sufficient to kill the worker. It is perhaps not generally known that, at high enough temperatures, carbon tetrachloride and trichloroethylene, both noninflammable, widely used solvents, will generate phosgene, a dangerous chemical lung irritant producing delayed pulmonary edema. Maloof[243] presented an unusual case of burns produced by trichloroethylene vapors at room temperature.

McDonald and McIntosh[244] call attention to the fact that dangerous amounts of hydrogen sulfide may exist in wells. They report 3 accidental deaths from this gas occurring when men were cleaning the well, which was part of the water supply of a vegetable-packing plant. The hydrogen sulfide, arising from decaying vegetation was found to be about ten times the safe level and acted as an immediate respiratory depressant. Ahlborg[245] reports less serious results of hydrogen sulfide exposure in the Swedish shale-oil industry, in which there is a high concentration of sulfur in the shale layers. Ahlborg describes loss of consciousness for short periods, as well as disturbance in balance.

Hardy and Maloof[246] report symptoms in 8 workers of an unknown total exposed to tetryl during explosive manufacture in World War II. One worker suffered definite disability, and in 2 cases death followed cirrhosis of the liver. The authors point out that the work had been discontinued at the end of the war, and the fatal cases were only by chance linked through epidemiologic evidence to the tetryl exposure. Hardy and Maloof think this may explain the few accounts of such cases in explosive manufacture. On the other hand, Bergman[247] reports that in his ten years' experience he found no case of even "suspected constitutional poisoning due to tetryl."

Certain industrial laboratories have recently found use for boron hydrides. Rozendaal[248] reports 4 cases of chemical engineers exposed for short periods in whom a syndrome-like, metal-fume fever developed. Accompanying this was evidence of irritation of the central nervous system if the exposure was to pentaborane. In 1 case a marked increase in blood boron was demonstrated. There was complete recovery in all cases.

Summary

An analysis of recent pertinent literature in the field of occupational diseases is presented. The point of view of this report is that considerable data exist to aid the clinician in establishing correct etiology and care in many occupationally related syndromes.

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MEDICAL INTELLIGENCE

BLADDER DISTURBANCE DUE TO APRESOLINE*

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THE usefulness of I-hydrazinophthalazine (Apresoline) in lowering the blood pressure of hypertensive patients is well established.[1]

However, side effects have been observed, such as occipital headache, tachycardia, palpitation, dizziness, weakness, nausea, vomiting, as well as (less frequently), numbness and tingling of the extremities, flushing, varying degrees of nasal congestion, lacrimation and conjunctival inflammation. Rarely, skin rash and fever have been reported.[2] As therapy with Apresoline is continued, these side effects generally subside and are persistently troublesome enough to cause discontinuance of therapy in only a few cases.

This report describes the part that Apresoline may play in causing difficulty in voiding with hypotonicity of the bladder and poor maximum voluntary voiding pressure. Perusal of the available literature, as well as correspondence with the Research Department and Division of Clinical Investigation of Ciba Pharmaceutical Products, Incorporated,[3] has revealed no published report citing urinary retention as a side effect from Apresoline alone, although it has been reported with hexamethonium.[2]

CASE REPORT

A 58-year-old married woman entered the hospital on May 7, 1952, for surgical exploration of a large firm mass in the lower abdomen rising out of the pelvis. Previous work-up had excluded the gastrointestinal and genitourinary tracts as the source of the lesion.

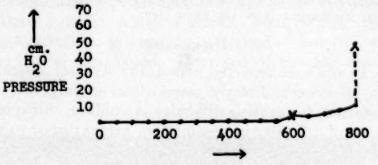
Prior to admission, the patient's blood pressure had been maintained at mildly hypertensive levels, so that on admission it was 160/90. Therapy up to that time had consisted of sedation, reassurance, a salt-free diet and Nitranitol. She had suffered a cerebrovascular accident 7 years before admission. She had had hypertension for 15 years.

There were no urinary symptoms, and the patient was otherwise in good health. Menses had ceased at 47 years of age, and there had been no bleeding since. The urine and the blood urea nitrogen were normal.

On May 8 a total hysterectomy, with bilateral salpingo-oöphorectomy for bilateral ovarian carcinoma, was done by one of us (S. H. C.). The neoplasm was attached to the posterior surface of the bladder and to the rectosigmoid. A Foley catheter was left indwelling.

On the 2d postoperative day, the Foley catheter was removed, and the patient voided well during the next 8 days.

On May 15, Apresoline in a dosage of 25 mg. 4 times a day was begun because of an alarming postoperative rise in the blood pressure, which averaged 200/105. It is of interest that while on Apresoline, the patient had a drop in blood pressure such that the highest systolic pressure was 170 and the highest diastolic pressure was 84, and the average blood pressure was 160/82. The Apresoline was continued thus until May 21, when, after the first cystometry, it was discontinued.

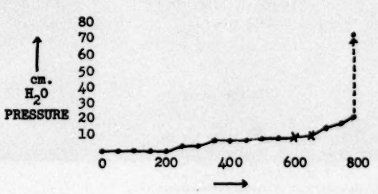


RESIDUAL URINE	325 cc.
FIRST DESIRE TO VOID	600 cc.
MAXIMUM CAPACITY	800 cc.
MAXIMUM VOLUNTARY PRESSURE	45 cm. H_2O

FIGURE 1. *Cystometrogram in a Patient Receiving Apresoline.*

X-ray examination of the chest on May 16 was negative, and excretory urography on May 17 was normal. The blood urea nitrogen on May 19 was 15.5 mg. per 100 cc.

On May 18, after being on Apresoline for 3 days, the patient first began to complain of bladder symptoms, referring to pressure over the bladder area 1 or 2 hours after she had taken the "green pill" (Apresoline). She had a frequent desire to void but difficulty in starting the urinary stream. This was the first time she had ever experienced such symptoms.



RESIDUAL URINE	20 cc.
FIRST DESIRE TO VOID	650 cc.
MAXIMUM CAPACITY	775 cc.
MAXIMUM VOLUNTARY PRESSURE	>72 cm. H_2O

FIGURE 2. *Cystometrogram Two Days after Apresoline Had Been Stopped.*

On May 20 residual urine, after 300 cc. had been voided, was 325 cc. Repeated residual urines obtained during the rest of the day were all over 100 cc.

On May 21 the first cystometry was done (Fig. 1). This showed a hypotonic bladder with poor maximum voluntary pressure.

After the cystometry, the Apresoline was discontinued. The patient experienced subjective relief of the urinary symptoms 12 hours later, and the relief continued.

On May 23, 48 hours after the Apresoline had been discontinued, the cystometry was repeated. This showed a return

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toward the normal curve, with normal maximum voluntary voiding pressure (Fig. 2). The residual urine at this time was only 20 cc.

To make the urologic work-up complete and to determine the presence of bladder or urethral disease, or both, immediately after the second cystometry, the patient was taken to the cystoscopy room, where cystography was done. This was followed by observation cystourethroscopy, all without anesthesia, analgesia or preoperative medication.

The cystogram was normal. Cystoscopy showed an ecchymotic area extending across the floor of the bladder and the proximal portion of the trigone, but did not involve either ureteral orifice. The patient, who had no urinary symptoms, was discharged later the same day.

Discussion

In the case reported above, the Apresoline seems to have been directly responsible, in large or full measure, for causing difficulty in voiding. All symptoms of difficulty in voiding, not present prior to the use of Apresoline, were relieved about twelve hours after the Apresoline had been stopped, and remained relieved, with no further treatment. Cystometry during Apresoline therapy showed a severely hypotonic bladder, with poor maximum voluntary voiding pressure; two days after the Apresoline had been stopped, the curve approached normal, with normal maximum voluntary pressure.

It is believed that the previous operation had not caused any difficulty in voiding since the patient voided normally from the second to the tenth postoperative day, or until three days after the Apresoline was started. She had noted no further urinary difficulty when seen six weeks after discharge.

Summary

A case in which I-hydrazinophthalazine (Apresoline) was apparently responsible for bladder difficulty is reported. The bladder disturbance disappeared when the administration of the drug was stopped.

11 Pearl Street

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DOCTORS AFIELD

Leonard Wood

Charles H. Bradford, M.D.*

Boston

In 1884, Leonard Wood was launched on a career of greatness by being fired. He was an intern at the Boston City Hospital at the time. Regulations forbade house doctors from performing even minor operations without formal permission, but Wood disregarded the formality in a case of a simple skin graft. The superintendent ordered his dismissal, and although the visiting surgeons submitted a written protest, with high commendation of Wood, his punishment was approved by the trustees. From his office, the superintendent watched Wood walk out of the institution, and remarked, "There goes a young man who will never come to any good."[1] The incident was typical of Wood's whole career. The only authority he ever thought he really needed was to be right.

Wood entered practice, succeeded in a small way, yearned for adventure in a large way, entered the Army as a contract surgeon and, on request for active service, was sent to Arizona, where the most strenuous and the last of the great Indian campaigns was about to begin. For years the Apaches, under Geronimo, had defied the United States Army, pillaged the countryside and murdered and tortured their victims. Over 800 ranchers had been killed. Wood joined Captain Lawton, of the Fourth Cavalry, and set out to track down the Indians across their native mountains and deserts until sheer exhaustion forced them to capitulate. In the twenty-month campaign that followed, he became known as "one of the few men who could ride, run, or walk down an Apache."[2] When line officers gave out, Wood substituted for them. Geronimo finally surrendered in 1887. Wood was awarded the Congressional Medal of Honor.

After the campaign, he became one of the very successful practitioners in the city of Washington, if success may be measured by the character of a doctor's clientele. Besides cabinet officers and prominent officials, two Presidents of the United States adopted him as their family doctor — Cleveland and McKinley. Wood made the acquaintance of a new, young friend: Theodore Roosevelt. Together they foresaw the impending war with Spain, and they planned to be in it. Their opportunity came when Congress authorized a new regiment, the First Volunteer Cavalry, soon known as the Rough Riders. Wood was assigned to the colonelcy. His old frontier comrades, ranchers and cowboys, flocked to serve under him. Roosevelt, as lieutenant colonel and second-in-command, attracted adventure-seeking college boys from the East; in later years, O. Henry described the regiment as composed of "the aristocracy of the wild men of the west; and the wild men of the aristocracy of the east."

Wood achieved an unbelievable record for speed in organizing this regiment. He recruited the men, equipped them, drilled them, transported them to Cuba and led them with brilliant success in combat at Las Guasimas — all in the space of forty-seven days.

Military victory was one of the least significant aspects of the Cuban campaign. The real glory grew from administrative triumphs. This was Wood's greatest achievement. After hostilities

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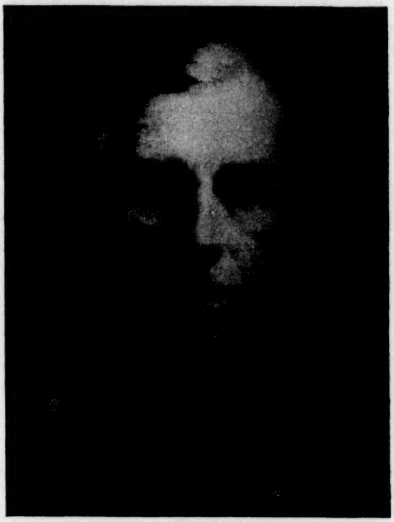
ceased, President McKinley appointed him governor general of the island. The job looked impossible. Wood set about to clean the cities. He paved the roads and rebuilt and extended the railroads. He developed a national system of public education. He instituted local self-government, established a native constabulary, organized law courts and arranged a constitutional convention. He resurrected and refinanced the economy and reduced the ravages of disease to a reasonable minimum. All this was done so effectively that within four years, a new Cuba had been created, and was given back to its native population as an independent country. The young man who would never come to any good was not yet forty-three.

As governor, Wood played a leading part in the work of the Yellow Fever Commission. He had urged the appointment of a board of experts to study the disease, and when Walter Reed and his heroic group were sent to Cuba in response to this appeal, Wood obtained the funds to prosecute their researches. When they reached the point where human experimentation became essential for a final proof, it seemed certain that officials in Washington would withhold permission, but Wood never asked for it. With scrupulous care, he laid down the conditions for volunteering, and then authorized the experiments on his own responsibility. Dr. Rixey, a well known Army surgeon, wrote: "When history has forgotten General Wood the soldier, and Governor Wood, the administrator, it will still remember Dr. Wood, the surgeon who conquered yellow fever."[2]

In 1902, by invitation of the Kaiser, Wood attended maneuvers of the German Army, and there he formed the conviction that a world war was inevitable. He started, even then, to preach preparedness but could do little about it. Instead, he campaigned vigorously in the Philippines, and established peace among a fiercely hostile population. In 1910 President Taft made him chief of staff. Still aiming at preparedness, Wood attempted to renovate the entire military establishment. He closed obsolescent Indian forts and brought the Army east for battle maneuvers; he revitalized officers' promotions, started courses for training civilians and reviewed the *Manual of Courts Martial*. He introduced new weapons, such as the hand grenade and the shot gun, and later the standard carbine, and the Lewis machine gun; he revived bayonet drill, which had been neglected. Only six years after the flight at Kitty Hawk, he insisted on an aircraft department for the Army. "Sooner or later," he said, "the aeroplane will be the greatest factor of the century in world affairs."[3] Slowly, he had molded the framework of an up-to-date army.

No man can make a life-long policy of progress and reform without arousing bitter opposition. Wood had become explosively controversial as Governor of Cuba, and so he remained. The formidable soundness of his conduct repelled critical onslaughts; behind this, he received staunch support from three presidents. As the war that Wood had predicted drew near, Wilson's pacifist administration assumed power, and Wood's influence ended. He was transferred to a subordinate departmental command, but even here, he urged "preparedness" until it became a byword. At Plattsburg, he inaugurated extremely successful officers' training camps, but he was officially reprimanded for his zeal. He submitted a basic selective-service plan, which the administration grudgingly accepted — but it refused to accept Wood. Deprived of the top command, he was offered a humiliating choice of training assignments. In the face of spiteful jealousy, he showed some of his finest traits of character. "I am a soldier," he said, "and go where I am sent." His superlative work in training the 84th Division in Kansas was rewarded by his being relieved of command when the troops embarked to win battle honors overseas. "Leonard Would, but they won't let him," the papers commented.



In 1920 the public wanted Wood for the presidency — at least, he won and held a large lead at the Republican convention over his nearest rival, Governor Lowden. However, a coalition of politi-

cal enemies succeeded in blocking him, and Harding was nominated. Wood returned to the Philippines as governor, and he again displayed his administrative genius by eight years of far-sighted and constructive leadership.

Throughout this amazingly active career, Wood carried a physical handicap that would have incapacitated most men. In 1902 his head struck a chandelier, and a meningioma slowly developed. By 1908 this caused spastic paralysis of his left foot and occasional convulsive seizures. Both Weir Mitchell and Osler missed the diagnosis. An inadequate operation was performed by a Boston surgeon in a house at 2 Louisburg Square. Two years later, Cushing successfully resected the tumor. Complete relief resulted for a number of years, but gradually the tumor recurred. Wood refused to yield time for further treatment until he was almost completely disabled in 1928. Cushing canceled a vacation in Europe to operate again. This time the tumor had reached the size of a lemon, and though it was successfully removed by an operation lasting eight hours, postoperative hemorrhage developed in the ventricles. "So ended the life of a gallant man. . .," Cushing[4] regretfully commented, believing that a two-stage operation might have succeeded.

The best summary of Wood's career is provided by his own comments when a staff officer, Major Eric Wood,[2] asked him the rules of his life. He replied:

> Always volunteer, no matter how dangerous or unpromising the task. Once you have volunteered, never stop fighting. Do things, and don't talk about them. During the process you are likely to discover opportunity; eventually you can win through to a success. . .; and then you will have the pleasure of hearing un-enterprising men, who would never take a chance, allude to your achievements as due solely to luck and influence.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38401

PRESENTATION OF CASE

A twenty-five-year-old man entered the hospital because of weakness and fever.

Although at the time the patient was in the fifth grade a physician had noted a heart murmur, he had enjoyed vigorous good health as a boy and had not had to limit his activity. During World War II he had attempted to enlist in the Marines, but after considerable debate he was rejected because a heart murmur was again noted. Fifteen months prior to entry, when he was examined by a physician because of headache, fever, weakness and cough of a few days' duration, a Grade III, rough, systolic murmur, which was loudest in the second intercostal space to the left of the sternum, was heard, but there were no signs of focal infection; penicillin was given for two days, and the patient did not return for follow-up examination. Four weeks prior to admission because of severe caries he had his upper teeth removed, five at a time; during the second visit he told the dentist that he had a heart murmur. Shortly thereafter he felt "all dragged out," and it was noted that he had a poor color and that he had a late-afternoon temperature rise to 100 to 101°F. He continued to work but finally consulted his physician one week prior to entry because of increasing fatigue. Examination at that time showed a well developed, well nourished, somewhat sallow-complexioned man. The upper gums were irritated and edentulous. The throat was injected. The carotid arteries pulsated visibly, and intercostal pulsations could be felt. The maximum cardiac impulse was forceful; its point was located 2.0 cm. outside the midclavicular line in the fifth interspace. There was a Grade III, long, harsh, systolic murmur, heard loudest just to the left of the sternum in the second interspace. A similar Grade II murmur was heard posteriorly at the tip of the left scapula. A low-pitched, long diminuendo, Grade II, blowing diastolic murmur was heard anteriorly, being loudest in the fourth interspace just to the left of the sternum. There were no palpable abdominal organs

or masses. No femoral, popliteal, dorsalis-pedis or posterior-tibial pulses were felt. There was no clubbing or other changes in the fingers. Scattered over the arms and legs were a number of small brownish spots. The temperature was 102°F., the pulse 90, and the blood pressure in the arms 164 systolic, 100 diastolic; the blood pressure could not be recorded in the legs. After two days of penicillin therapy the patient felt better subjectively but continued to have a low-grade fever. Two days before admission the white-cell count was 10,700, with 71 per cent neutrophils, and the sedimentation rate was 60 mm. in one hour uncorrected.

On admission to the hospital he complained of generalized weakness and occasional chilly sensations. The gums of the upper jaw were healed, the throat was still moderately irritated. Examination of the fundi showed prominence and narrowing of the arterioles with arteriovenous nicking. The lungs were normal. The diastolic murmur was perhaps slightly louder, but otherwise the examination was unchanged.

The temperature was 102°F., the pulse 100, and the respirations 20. The blood pressure was 138 systolic, 106 diastolic.

Examination of the blood showed a hemoglobin of 86 per cent and a white-cell count of 11,600, with 85 per cent neutrophils. The urine had a specific gravity of 1.015 and was normal. A blood Hinton test was negative. A blood culture showed no growth. Roentgenographic examination of the chest demonstrated considerable enlargement of the heart in the region of the left ventricle and slight dilatation of the ascending aorta. The lung fields were clear, and the diaphragm low. There was notching of the undersides of the ribs (Fig. 1).

The temperature fluctuated from normal each morning to a peak of 101 to 102°F. each afternoon. Four blood cultures taken at the time of the temperature peaks yielded no growth. During the hospital stay no new symptoms developed except for nausea and vomiting on one or two occasions. The patient was discharged unimproved on the seventh hospital day for penicillin therapy at home.

The patient received 600,000 units of penicillin intramuscularly twice daily. Two days after discharge he felt well in the evening and apparently slept soundly during the night. On the following morning his family heard him snoring loudly and found him comatose. Ten minutes later he died.

Differential Diagnosis

Dr. Gordon S. Myers*: After I had read over the protocol, it seemed perfectly clear that this patient had coarctation or atresia of the aorta. Many typical features of the disease were present. In the first place the patient was a male. Coarctation of the aorta occurs about five times more often in males than in females. Secondly, there were easily palpable intercostal pulsations. There was hypertension in the arms and hypotension in the legs. The present evidence suggests that diastolic hypertension in coarctation of the aorta is due to diminished renal blood flow, which in turn results in a general increase in peripheral resistance. Sometimes there is almost as much elevation of the diastolic pressure in the legs as in the arms. However, the systolic pressure is usually much higher in the upper, as compared with the lower part of the body. The systolic hypertension is due to discharge of the stroke volume of the heart into an arterial reservoir of diminished capacity and often of diminished elasticity as well, since these patients have premature arteriosclerosis. Finally, there was a systolic murmur, first detected in childhood, that was best heard to the left of the upper sternum but was also heard posteriorly. Sometimes the murmur of coarctation of the aorta is loudest over the upper spine. Anteriorly, the murmur is usually best heard to the left of the upper sternum, as in this case. There may be some extension of the murmur into diastole because there is blood flowing through the coarcted segment of aorta in diastole as well as during systole. Sometimes, systolic murmurs continuing into diastole are heard over various parts of the chest, probably owing to flow of blood through the dilated tortuous collateral channels.

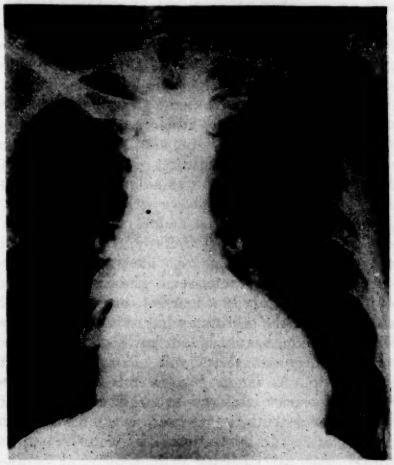

Figure 1.

This patient was noted to have a Grade II, early, diminuendo, diastolic murmur to the left of the lower sternum. This seems best explained by the

*Assistant physician, Massachusetts General Hospital.

presence of a bicuspid aortic valve, which coexists with coarctation of the aorta in about 40 per cent of cases and which is not infrequently the site of bacterial infection or rheumatic endocarditis. Is there any other possible cause for such a murmur? On rare occasions, coarctation may be associated with subaortic stenosis, giving rise to a systolic and diastolic murmur. However, the description of the murmurs does not suggest this diagnosis in the patient under discussion.

What did the patient have in addition to coarctation of the aorta and a bicuspid aortic valve? It seems to me that he most certainly must have had a bacterial infection involving either the bicuspid aortic valve or the aorta itself in the region of the coarctation. To be sure, he did not have any clubbing, splenomegaly, microscopic hematuria or clear evidence of petechiae. Some brown spots were noted on the skin of the arms and legs, suggesting freckles or some type of pigmentation rather than petechiae. The blood cultures were negative, but the patient had received penicillin prior to admission to the hospital. We have seen that in cases of proved subacute bacterial endocarditis, even without previous antibiotic therapy, repeated blood cultures have been negative. The history in other respects is quite characteristic. The illness followed tooth extraction. It is of interest that patients with coarctation of the aorta may have enlarged arteries, with perhaps increased blood flow to the jaws, and may exhibit prognathism and relative increase in dental pulp. As far as I know this does not predispose to caries. In any event, the patient had carious upper teeth, which were extracted without prophylactic administration of penicillin — protection that all patients with congenital cardiovascular disease should have under these circumstances. Soon after the tooth extraction, he suffered from malaise, pallor, fatigue and fever. The sedimentation rate was elevated, whereas the white-cell count and differential were relatively normal, findings that are quite typical of subacute bacterial endocarditis uncomplicated by embolic phenomena with infarction. Finally, I can think of no other very reasonable cause for the fever in this case. To be sure, such patients may have rheumatic fever.

It seems profitless to discuss other possible causes for fever of undetermined origin. After a brief period of study in the hospital, the patient was sent home on penicillin treatment but was given a dosage that would now be considered inadequate, particularly since the type of organism and its sensitivity were not known. Presumably, the clinical diagnosis was subacute bacterial endocarditis. Shortly after returning home, he died rather suddenly without medical observation at the time; therefore, the immediate cause of death can be only a matter of speculation.

In the past, patients with coarctation of the aorta who died of causes directly related to this disease have had one of several complications. About half have died of congestive heart failure or of subacute bacterial endocarditis. I do not believe this patient died of congestive heart failure or of the infection per se. About a third have died of rupture of the aorta, usually of the ascending aorta, where there is often aneurysmal dilatation, but sometimes of the descending aorta below the coarctation. The latter occurs less frequently but is more likely to happen if there is bacterial endarteritis. Sometimes, aneurysms of the intercostal arteries at the point where they join the aorta are the site of the rupture. Other patients with coarctation have died of a cerebrovascular accident, usually hemorrhage from an aneurysm of one of the cerebral arteries, which in patients with bacterial endocarditis may be mycotic in origin. Cerebral embolism may occur secondary to a bacterial endocarditis or as the result of thrombus formation in a dilated portion of the aorta. The patient under discussion was found comatose and survived for at least ten minutes after the occurrence of the terminal accident. Although it is merely a guess, I believe he had a cerebrovascular accident from hemorrhage or possibly from an embolus.

May I see the chest x-ray film?

DR. CHIU-CHIEN WANG: These films show some enlargement of the heart principally in the region of the left ventricle and some prominence of the ascending aorta. I cannot trace the descending aorta very well on this film. The lung fields appear to be clear. The diaphragm lies somewhat low in position. There are obvious notching deformities of the undersides of the ribs on both sides (Fig. 1).

DR. MYERS: Do you see any calcium in the region of the aortic valve?

DR. WANG: I do not see any with certainty.

DR. MYERS: Was an electrocardiogram taken?

DR. H. S. HARVEY: No.

DR. MYERS: In summary, I believe this patient had coarctation or atresia of the aorta, with a bicuspid aortic valve, hypertensive heart disease, subacute bacterial endocarditis involving the bicuspid aortic valve or the aorta and finally either rupture of a cerebral aneurysm or cerebral embolism leading to death.

A PHYSICIAN: Do you think a rupture of the aortic cusp could cause immediate death?

DR. MYERS: I suppose it is possible; the patient was found to be comatose, and no statement was made about any respiratory distress or evidence of acute left-sided heart failure, all of which make it impossible for me to make that diagnosis.

DR. BENJAMIN CASTLEMAN: This patient was not a patient in the Massachusetts General Hospital but was in one of the suburban hospitals for which we supply the pathology service. Dr. Harvey took care of this patient in Concord. Do you have any comment?

DR. HARVEY: The striking thing was that during the three or four days prior to death, there was no particular change in the symptoms or complaints.

DR. MYERS: That fact would lead me to suspect that perhaps the terminal event was rupture of the aorta. Rarely, that is a chronic affair that is due to a very slow leak similar to what may occur with a dissecting aneurysm, and it is usually associated with similar symptoms. Such patients usually complain bitterly of pain. One patient, whose rupture began twelve days before death, shot himself. A few patients have survived for a longer time after a partial rupture or dissection of the aorta.

CLINICAL DIAGNOSES

Subacute bacterial endocarditis.
Coarctation of aorta.
Myocardial infarction.

DR. MYERS' DIAGNOSES

Coarctation of aorta.
Bicuspid aortic valve.
Subacute bacterial endocarditis of aortic valve or aorta.
?Ruptured cerebral aneurysm.
?Cerebral embolus.
Hypertensive heart disease.

ANATOMICAL DIAGNOSES

Coarctation of aorta.
Subacute bacterial endocarditis of bicuspid aortic valve.
Mycotic aneurysm of aortic valve, with rupture.
Hemopericardium.
Myocardial infarct, recent.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: As Dr. Myers predicted, there was coarctation of the aorta and a bicuspid aortic valve. The coarctation was located just beyond the orifice of the left subclavian artery, and although at first we thought there was a complete sealing off of the aorta, we were able to find a lumen less than 0.5 mm. in diameter. The bicuspid aortic valve was calcified and was the site of a bacterial endocarditis that had produced a mycotic aneurysm of the aortic wall of the sinus of Valsalva, which had then ruptured to produce a hemopericardium. The mycotic aneurysm had formed slowly, was filled with thrombus and measured about 3 cm. in diameter. We had one case like this about fifteen years ago without coarctation of the aorta but with subacute bacterial endocarditis on a bicuspid aortic valve; exactly the same type of mycotic aneurysm had formed, ruptured and produced death.*

DR. MYERS: Do you think the rupture occurred at the time of death? There was no chronic dissection?

DR. CASTLEMAN: There was no dissection.

DR. MYERS: Was an examination of the brain done?

DR. CASTLEMAN: No.

DR. THOMAS PAINE: What was the infecting organism?

DR. CASTLEMAN: We did not have a post-mortem culture; the blood cultures before death did not grow out organisms. The mycotic aneurysm that was filled with organized thrombus was large and firm enough to compress the perfectly normal-appearing left descending coronary artery to lead to a very acute myocardial infarct.

DR. MYERS: How long do you think the infarction had been present?

DR. CASTLEMAN: Probably for three or four days.

DR. MYERS: Could it have happened prior to discharge from the hospital?

DR. CASTLEMAN: Yes; it must have.

DR. MYERS: An electrocardiogram might have helped in making that diagnosis.

DR. HARVEY: The patient had no change of symptoms in the last three or four days to make us suspect infarction.

CASE 38402

PRESENTATION OF CASE

A sixty-three-year-old woman entered the hospital because of bloody diarrhea.

The patient, who had enjoyed robust health, suddenly began to have nausea, diarrhea and fever three weeks prior to admission; she did not vomit. For a week she had three or four daily loose movements of dark-brown feces, which contained streaks of both fresh and changed blood; this was accompanied by a vague discomfort in the left lower quadrant and a feeling of distention that was relieved somewhat by belching or bowel movements. During the subsequent two weeks the diarrhea became less noticeable; a few flecks of blood remained in the stool, and occasional left-lower-quadrant pain was noted. However, during this time she lost 10 pounds in weight. There was no actual visible distention, crampy pains, vomiting, massive bleeding, tenesmus, narrowing of the stool caliber or tarry stools. On the afternoon of admission the patient suddenly began to have frequent urgent bowel movements, which were accompanied by tenesmus, mild, crampy left-lower-quadrant pain and a feeling of weakness. The feces contained at first fresh blood and later a mixture of fresh and clotted blood.

For the ten years prior to entry the patient had mild constipation and took a cathartic every second or third day. There was no history of rheumatic fever, angina, ankle edema, dyspnea, orthopnea, food intolerance or previous diarrhea or melena. She was apparently a very stoical person, but she allegedly had made vague references to abdominal pains to her friends for a number of months before admission.

Physical examination revealed a very pale woman. There was no venous congestion. The chest was clear. The heart was slightly enlarged, and a Grade

*Case Records of the Massachusetts General Hospital (Case 21231). *New Eng. J. Med.* 212:1090-1092, 1935.

II systolic murmur was heard over the entire precordium. The abdomen was soft, and no masses were palpable, but there was diffuse tenderness on palpation in the left lower quadrant. Constant hyperactive peristaltic sounds were heard on auscultation. No masses were felt on rectal examination, but dark-red blood was present on the examining finger. Pelvic examination was negative.

The temperature was 99°F., the pulse 80 and slightly irregular, and the respirations 20. The blood pressure was 115 systolic, 70 diastolic.

The urine was normal. Examination of the blood disclosed 9 gm. of hemoglobin and a white-cell count of 9300. The nonprotein nitrogen was 23 mg., and the total protein 5.0 gm. per 100 cc.; the prothrombin time was 15 seconds (normal, 14 seconds). Sigmoidoscopic examination revealed an area of narrowing 18 cm. above the anus, beyond which the scope could not be passed and which could not be dilated with air; the mucosal pattern of the rectum was normal. A barium-enema examination showed no gross defects within the colon except for multiple diverticula in the sigmoid colon; there were no associated signs of inflammation. Barium filled the entire colon and refluxed into the terminal ileum without difficulty. There was good emptying of barium from the colon. The mucosal folds of the descending colon appeared to be slightly thickened; in other areas it was not remarkable. A roentgenogram of the chest showed clear lung fields, a tortuous calcified aorta and a slightly prominent left ventricle. An electrocardiogram showed auricular premature beats and nonspecific T-wave changes; the pattern was not diagnostic of a definite abnormality.

The rectal bleeding subsided during the first three days in the hospital but recurred a week later and persisted. A repeat sigmoidoscopic examination again demonstrated an obstruction to the passage of the scope about 18 cm. above the anus where the lumen was narrowed to a diameter of approximately 0.5 cm. A definite organic stricture could not be demonstrated at this point, and the observer believed that the narrowing most probably represented spasm. The mucous membrane at this level was edematous and reddened and tended to prolapse into the lumen; below this level there was no abnormality. The patient continued to pass blood by rectum. On the fourteenth day an operation was performed.

Differential Diagnosis

Dr. Warren Point*: This patient had ten years of mild constipation and then a sudden onset of left-lower-quadrant inflammation with bloody diarrhea. Further examination revealed a normal rectum and an apparently spastic area 18 cm. above the anus, at which point the mucosa was reddened and edematous. X-ray examination revealed no filling defect, with satisfactory emptying; there was no stricture. Hence I must call the narrowed area "spasm," rather than true cicatricial, or neoplastic, stricture. Contrary to the x-ray interpretation in the record, the films that were given to me with the protocol revealed "amputation" of diverticula in the sigmoid, and this, with thickened mucosal folds in the descending colon, is adequate evidence of inflammation of some type. This interpretation is confirmed by the sigmoidoscopic picture of spasm and edematous, reddened mucosa.

I am satisfied that the barium enema and the sigmoidoscopic examination together gave an accurate picture of the lower bowel. There is no evidence that disease existed elsewhere to explain the symptoms, since all signs pointed to the left lower quadrant.

What pathologic entities could account for this picture? Ulcerative colitis is not suggested by the sudden onset in a patient of this age, the lack of ulcerations by x-ray and direct examination, and the whole clinical picture. Amebiasis is fairly well ruled out by the course of the disease, the fever and the intense localization. The last would presuppose an amebic granuloma, which is not suggested here. Lymphopathia venereum may produce a rectal stricture, but this was not a stricture, nor was it the chronic course of this venereal disease. Bacillary dysentery of such severity would produce an intense, diffuse inflammation of the entire colon, and there would be no sparing of the rectal region. Benign polyps may bleed massively at times, but it is unusual. Certainly, fever and inflammation would be highly unusual. The same reservation holds for any other potential bleeding lesion, such as angioma. There was no evidence for lymphoma, malignant melanoma, tuberculosis and so on.

Carcinoma must be considered. This is a fairly common cause of rectal bleeding and change in bowel habits such as this patient described. It is probably the most common cause of rectal bleeding in older patients if we except hemorrhoids. Perforation of the tumorous colon may produce an abscess with attendant signs of leukocytosis, fever and tenderness. Ulceration of the tumor may cause bleeding.[1] Intermittent, spontaneous diarrhea may alternate with constipation in about 20 per cent of the cases of carcinoma of the descending colon, despite the fact that it is much more common to have constipation and obstructive symptoms. It is difficult to accept this diagnosis, however, because adequate examination of the bowel failed to reveal any sign of a filling defect or a mass. Obstructive spasm below a carcinoma is rare; if the growth is within reach of the sigmoidoscope, it should be seen easily. According to Bockus,[2] this is an important point in differentiating carcinoma from diverticulitis of the sigmoid colon.

Diverticulosis was most certainly present in this patient, and I believe there is adequate evidence of diverticulitis, with spasm, tenderness, fever, diarrhea, mucosal edema and "amputation" of several of the pockets. This indicates nonfilling of the pocket itself, with partial filling of the neck — a condition

*Assistant in medicine, Massachusetts General Hospital.

seen with an inflamed or narrowed entrance to a diverticulum. Sigmoidoscopic examination is rarely diagnostic for diverticula, but contracture or spasm is commonly seen in the presence of inflammation. The inflamed section of bowel may be rigid and angulated. These findings are also confirmed by x-ray examination in many cases.

Bleeding from diverticula has been a controversial subject for many years. This point is now fairly well accepted. Willard and Bockus[3] found gross bleeding in 5 of 72 cases of diverticulosis. The danger in accepting this theory is that diverticulosis is quite a common disease in the older age group, and the physician must not let the known presence of diverticula blind him to the possible presence of other bleeding lesions. There is no reason to believe that diverticulosis predisposes to the development of carcinoma.

In conclusion, I believe that this patient had diverticulitis of the sigmoid colon, the most common and usually the only symptomatic location. The operation performed was probably local resection of the involved sigmoid, possibly with a preliminary colostomy to divert the fecal stream and promote healing before a direct attack upon the involved area. Whether this was necessary is dependent upon the degree of local sepsis. Since no mention is made in the protocol of continuing high fever, and since fourteen days elapsed before operation, I assume that it was a primary resection. This should have been adequate time to prepare the infected bowel for operation.

I cannot rule out an incidental carcinoma that produced bleeding, but there is no evidence for this, and I have abundant evidence for significant diverticulitis of such a degree as to produce gross bleeding. I shall, therefore, confine my diagnosis to diverticulitis of the sigmoid colon.

Clinical Diagnosis

Diverticulitis.

Dr. Point's Diagnosis

Diverticulitis of sigmoid colon.

Anatomical Diagnoses

Chronic ulcerative colitis, localized to sigmoid.
Diverticulosis.

Pathological Discussion

Dr. David Kahn: This case, I fear, had a number of diagnostic "blind spots." The only sure way of making a diagnosis was by operation. The preoperative clinical diagnosis was diverticulitis. After a preliminary transverse colostomy, 48 cm. of descending and sigmoid colon was removed. Numerous small diverticula were present but these all had wide necks and showed no evidence of diverticulitis or peridiverticulitis. There was a 12-cm. segment of the bowel that was indurated and thickened; this began 7 cm. from the distal resected edge. The mucosa in this area was irregularly ulcerated, the ulcers being irregular in shape and size, but being on the whole longitudinally disposed. There were only small areas of hyperemic mucosa separating these ulcers. The ulcers on the whole were shallow, had sloping edges and were not undermined.

Microscopical examination showed the depth of ulcers to vary, some involving only mucosa, and others mucosa and submucosa; a few penetrated to involve the superficial part of the inner muscle coat. The surface of many of the ulcers was covered by a thin coat of fibrin, and the floor was made up of a loose vascular connective tissue infiltrated by a varying number of lymphocytes and plasma cells and an occasional eosinophil. In others the ulcer surface was lined by a layer of flattened cells, and the floor composed of either vascular connective tissue or fibrous tissue resembling submucosa; this may have represented early healing. The muscle coat was somewhat thickened and hypertrophied and had some scattered fibrosis. A very occasional crypt abscess, as described by Warren and Sommers,[4] was found.

A new thought concerning ulcerative colitis has recently been suggested by Levine and his coworkers.[5] Using histochemical technics and phase microscopy, they demonstrated certain distinct changes in the basement membranes and intercellular connective tissue in the mucosa and submucosa in biopsy material removed from patients with ulcerative colitis. The changes were similar to those seen in the "collagen diseases," and these workers regarded the fundamental tissue reaction in ulcerative colitis as similar to that in this group of diseases. We examined sections stained by the periodic-acid Schiff technic, but the findings were equivocal. We were unable to find any constant basement-membrane change except in a few degenerated surface glands, or fibrinoid necrosis or vasculitis; the fact that we studied formalin-fixed material made interpretation of these stains somewhat less specific.

We found no evidence of tuberculosis, amebiasis or of any other specific cause for this ulcerative process and so must classify it as idiopathic ulcerative colitis. Whether this will remain as one of the less common varieties of ulcerative colitis, the localized type, remains to be seen; it may well spread to involve other parts of the large intestine. At the end of three months the patient appeared to be doing well, and sigmoidoscopic and barium-enema examinations were negative. It may be worth while to add here that our colleagues in the X-Ray Department inform us that, as Dr. Point has already pointed out, diverticulitis is rarely responsible for gross bleeding.

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CALL TO ACTIVE DUTY

THERE is hardly a large hospital in the United States in which a significant segment of the resident staff is not in turmoil over the haphazard manner in which the doctor's draft is being administered. Undoubtedly, the disturbance will soon be reflected in serious difficulties for the professional staffs of hospitals and for medical schools charged with the care of patients and with clinical teaching of medical students. Many young physicians are being classified by their draft boards as 1A and thus are subject to being called to active duty. The difficulty is that no one knows when he will be called — next week, next month or next year. Most of these young men began their present appointments on July 1 and are expected, by either written or implied contract, to serve at least a full year in line with the general policies of the great majority of hospitals. Yet under present circumstances this carefully planned preparation for future military and civilian service may be interrupted at any time, and the functions of the hospitals disorganized to a greater or lesser extent.

Congress has seen fit to set certain limits to the size of the armed forces and to set the pace for the preparedness program of rearmament. Is it, therefore, too much to expect a reasonably planned and orderly call of valuable young men who are preparing themselves for a much needed and highly specialized service to their country? The armed forces undoubtedly require most of their medical strength for general duty, but they also need men to care for patients in general hospitals and in various specialties and consequently must utilize physicians with special training in almost all the medical and surgical fields. Is it unreasonable to expect that they should be able to estimate their requirements in each category periodically and well in advance, as civilian hospitals do? And could not these military requirements be relayed to the various local draft boards and to the medical advisory boards before the men who are needed for military duties are already committed to civilian posts? Certainly, it seems unnecessary to delay what should be an orderly process until they have already started in these positions and are thus difficult or impossible to replace.

During World War II a plan was evolved whereby the length of medical-school terms and hospital appointments, as well as the time of beginning such periods of training, were synchronized with the calls of the armed forces for young physicians to active duty. This was the so-called 9-9-9 plan, which allowed nine months for each year of medical-school work, nine months for an internship and one or, for some, possibly two additional periods of the same length of residency training. This plan maintained the continuity of the hospital medical services and at the same time provided the hos-

pitals and the armed forces with a certain number of better trained physicians and physicians trained in special fields. Largely as a result of this program the appointments in most hospitals are now made on an annual basis. These appointments begin on July 1, to synchronize with the time when the medical-school course is completed; the co-ordinated schedules of hospital house staffs are set up in advance on this basis.

If a man is called to service in the middle of such a year of training, a year of his professional life may be largely wasted. This is because most physicians returning from active service must start that year over again and often must wait for several months to obtain a suitable appointment if, as usual, they are separated from the military service at an intermediate date. Since the study of medicine has become so expensive, long and tedious and a large proportion of the men already have family responsibilities at a time when they can first embark upon their eventual professional careers, this waste of valuable time can hardly be called fair or reasonable. Nor can it be considered in the public interest to waste an important national asset of the future — a year of professional service for most doctors called to the colors.

Would it not be best for all concerned to give these young men the opportunity to begin their military service at the beginning of one of the regularly scheduled years of training and to end it at a time when they can proceed without delay to the orderly completion of their training? Would it not be to the greatest advantage of both the armed forces and the civilian population to have them serve at times planned and scheduled in advance? And, finally, is it not to the greatest advantage of the military services, the individuals and the community to defer a small proportion of properly qualified men for the additional two or three years required to complete special training so that, with economy, the needs of the armed forces in these specialties, as well as those of the civilian population, can be filled? These men, although few in number, occupy the key positions at the apex of the hospital programs for the training of many times their number of future medical officers.

To the uninitiated layman, it seems reasonable to expect a more rational and fairer approach to the manner in which physicians are called away from their civilian responsibilities. For two years, the machinery has been available to provide for an efficient military medical establishment without unduly disrupting the vital civilian functions of medical care, hospital service and medical education. Unfortunately the medical advisory boards either cannot or have chosen not to take the initiative in impressing upon the military services the importance of synchronizing their calls with the generally accepted periods of hospital training in such a manner as to be most advantageous to all concerned. The young men themselves are hardly in a position to bring to bear, out of their indignation, the necessary force of opinion. Should not the medical societies, hospitals and medical schools through their medical advisory boards set about now, before it is too late, to try to remedy this situation? Both the physicians themselves, once they receive their medical degrees and begin their clinical training, and the hospitals in which such training has become an integral part of the programs of medical care and teaching understand clearly that the required period of military service must be included in their over-all plans. What they refuse to accept cheerfully is that chaos should continue when an acceptable and workable plan is possible.

CLINIC FOR MAN-MADE DISEASES

THE progress report by Hardy in this issue of the *Journal* and that of September 25 points up the growing body of knowledge in the field of man-made diseases. An attempt has been made in the selection of clinical reports used in these articles to help the physician to an understanding of diagnostic possibilities in disease associated with modern occupational exposures.

This is an appropriate time to bring to the attention of the readers of the *Journal* the work of the Occupational Medicine Clinic at the Massachusetts General Hospital. This is an investigative project directed toward study of the correct etio-

logic relation between worker illness and hazardous operations. A recent survey found no comparable clinical activity in hospitals in this country.[1] However, groups and individuals such as the staff of the Kettering Laboratory at the University of Cincinnati and Spolyar of the Division of Industrial Hygiene in Indiana offer expert consultation in the field of occupational disease to their clinical associates. The Massachusetts General Hospital Clinic began its work in 1949 supported by a grant from the National Institute of Health, Research Grants Division, which has continued to the present.

The Massachusetts General Hospital has taken an interest in diseases of occupational origin since 1913, when Dr. David L. Edsall formed an industrial-medicine clinic. From that time until late in the 'twenties, cases thought to be of industrial origin were seen in the outpatient clinic under Dr. Wade Wright's direction. The visiting physicians of the hospital and the Social Service Department, under Miss Ida Cannon's guidance, participated actively in the work. During the 1920's definitive work in lead poisoning was done at the Hospital under the direction of Dr. Joseph C. Aub, supported by funds from the lead industries. With this background it has been quite natural for interest in occupational diseases to be renewed. Dr. Nathaniel W. Faxon and Dr. J. Howard Means gave generously of interest and support in launching the work that is now going on under the title of the Occupational Medicine Clinic.

The Occupational Medicine Clinic is greatly benefited by a close liaison with the Division of Occupational Hygiene of the Massachusetts Department of Labor and Industry. The chemists and engineers of the Division are able, in field and laboratory studies, to evaluate exactly the qualitative and quantitative hazard in the individual case under study. With such data correct occupational etiology can often be established. Also, unusual cases, or groups of cases, come to light through the activities of the physician and technical staff of the Division of Occupational Hygiene.

The work of the Clinic is divided into three categories. On Wednesday and Saturday mornings patients who have been referred for study are seen in the outpatient medical clinic. The cases may be diagnostic problems from community chest x-ray surveys or State tuberculosis sanatoriums. They may be problems in differential diagnosis from visiting physicians who are considering the possible industrial etiology of anemias, liver disease and vague gastrointestinal disturbances such as can be produced by chronic lead intoxication.

The second phase of the Occupational Medicine Clinic is the inpatient work, which depends on the character of the clinical material. The presence of certain industries, such as storage-battery manufacture, fluorescent-lamp manufacture, artificial-leather industry and, during the war years, explosive manufacture, in this community determines the kind of cases that appear for study. Patients with chronic beryllium poisoning from fluorescent-lamp manufacture continue to present themselves even though beryllium was discontinued in the manufacture of fluorescent lamps in May, 1949. The study of this disease is of great interest and importance because of the seriousness of the prognosis, the widespread systemic effects in persons affected and the continuing appearance of new cases. Since it was discovered that ACTH and cortisone had a transient, brilliant success as therapy in the treatment of beryllium disease, the Clinic has participated in the attempt to understand and evaluate the usefulness of these drugs. A study of a group of cases of lead poisoning at the Massachusetts General Hospital and at the Veterans Administration Hospital in West Roxbury has been undertaken to determine whether or not citrate salts are, as has been claimed, successful in the treatment of this disease. An interesting series of cases of pulmonary diseases of occupational origin was thoroughly studied with the help of basic pulmonary-function testing at the Department of Physiology of the Harvard School of Public Health and the Heart Station at the Boston City Hospital. An attempt has been made to treat some of these cases with intermittent oxygen therapy under pressure, as suggested by Motley and Tomashefski.[2] This is a worthwhile project in rehabilitating men with chronic respiratory disease to the point of returning them to employment.

A third important service of the Clinic is to answer consultations in all parts of the hospital and in other hospitals in this and other communities. This activity serves to create and increase interest in the problems of diagnosis and to bring to light proper problems for clinical investigation in occupational disease. There have been more than thirty such consultations in the last year, and it is hoped that the number will increase when it becomes known that the service is available.

From this description it can be seen that the work of the Clinic is a new, enthusiastic attempt to study the problem of etiologic relation and pathogenesis of injurious exposures in all types of occupations. An important sequel of the investigative and consultative capacity of the Clinic is the urge to communicate in informal teaching the present data and possible implications in clinical medicine of work-acquired intoxications. The problem of discovering appropriate clinical material has not been completely solved.

The skills and resources of the Clinic are available to any physician for consultation without charge to the patient. No dermatologic or surgical cases are accepted for study because of the services presently available in these fields and because of the interests of this project. However, diagnostic opinion of job relation is always available to any referring physician.

In this period of social change the questions posed by occupational hazards are of more than medical interest. It may be wisely urged that other teaching hospitals consider affiliation with State and university units skilled in the evaluation of toxic exposures to assist physicians in the diagnostic study of possible job-related illness. Meanwhile, physicians may avail themselves of the help offered by the Massachusetts General Hospital Occupational Medicine Clinic.

References

1. Brown, E. W. Undergraduate teaching of occupational medicine in American and Canadian medical colleges. *J. A. M. A.* 145:926-928, 1951.

2. Motley, H. L., and Tomashefski, J. F. Treatment of chronic pulmonary disease with intermittent positive pressure breathing. I. Evaluation by objective physiological measurements. *Arch. Ind. Hyg. & Occ. Med.* 5:1-9, 1952.

EARLY DETECTION OF PULMONARY CANCER

Elsewhere in this issue of the *Journal*, Bondi and Leites report the results of screening for intrathoracic malignant tumors of more than 200,000 persons living in the vicinity of New York City. Approximately 1 in each 1000 persons studied was found to have a previously unknown intrathoracic cancer, an incidence so low that the expense of case finding becomes prohibitive except when a cancer survey is undertaken as part of a program directed against tuberculosis. In the course of their analysis these authors were unable to follow up and confirm the provisional diagnosis in about a third of all suspicious cases. They made the following comment:

> The large number of undiagnosed cases in this series is striking and somewhat discouraging. In these cases the effort and expense of the survey were completely wasted. In most of them the diagnosis remained undetermined because of poor co-operation of the patient or unawareness and a conservative attitude on the part of the private physician. In contrast to the tuberculous, the person suspected of having cancer is not subjected to any pressure from the community to obtain diagnosis and treatment.

This comment, although true, is deserving of some qualification. Since the cancer detection was only an auxiliary part of the tuberculosis program the waste of effort and expense is to be evaluated in terms of tuberculosis screening as well as cancer detection. Moreover, it is proper that persons suspected of having cancer should not be subjected to undue pressure from the community to obtain treatment: unlike the patient with active tuberculosis the patient with bronchogenic carcinoma does not constitute a threat to the well-being of his fellows.

The decision whether to let nature quietly take its course or to submit to a major thoracic operation is in the last analysis a personal matter to be decided by the patient, his family and his physician. This decision is influenced by two major facts. In the first place the average age of male patients with malignant pulmonary tumors is close to sixty years. The oldest men whose tumors evaded direct inspection by the examiner were probably seventy or more years of age; some of them were in all likelihood influenced by having other infirmities associated with advanced years. Secondly, the authors stress the fact that long-term results of

therapy are still extremely poor, which undoubtedly influences the attitude of an elderly person told he is suspected of having cancer of the chest. More knowledge of the causes and ways of preventing pulmonary cancer is the truly necessary objective, one that comes a step closer with every analysis such as that reported by Bondi and Leites.

Until the ultimate goal of prevention as opposed to control is attainable, the objective of screening for cancer together with tuberculosis is shown to be worth while. The authors suggest that a broadening of cancer control could be attempted by x-ray examination of all patients admitted to general hospitals, in the hope of reaching a larger number of elderly people. One could considerably curtail the expense of any such procedure — so far as the specific purpose of cancer detection is concerned — by limiting mass examinations to persons more than fifty years old.

ELEVENTH POSTGRADUATE ASSEMBLY

THE present concern of the Massachusetts Medical Society with instruction in medicine stems from its very act of incorporation in 1781 and the first of the annual discourses, delivered in 1804. For its existence is based on the universal acknowledgment of the necessity of health to the happiness of society, of the close connection of "its preservation or recovery . . . with the knowledge of the animal economy and of the properties and effects of medicine," and of "the benefit of medical institutions, formed on liberal principles, and encouraged by the patronage of the law."

This concern has not been lost sight of in modern times when social, economic and political problems seem also to occupy so much of the interest of the Society and its multitudinous committees. For in 1938 the first of the annual New England Postgraduate assemblies was held — annual except for the war years — and in 1946 the nearly rival Committee on Postgraduate Medical Education started its celebrated courses of instruction designed especially for the reconditioning of returning medical veterans. These courses have outlived the supply of veterans, so far as quantity is concerned; ready to continue its good works, however, the Committee a year ago launched its Survey of Postgraduate Medical Education in collaboration with other pedagogic and benevolent agencies, and has now evolved its ambitious but realistic Postgraduate Medical Institute.

Like an older brother or even a heterologous twin, similar enough to cause perpetual confusion in the matter of differential identification, the Committee on Postgraduate Assembly — of the Massachusetts Medical Society, but acting for all the New England state societies — has continued to stage its nearly annual three-day intensive course each fall.

Held this year at the Hotel Statler, in Boston, the Assembly — the program of which appears elsewhere in this issue of the *Journal* — will include symposiums on thyroid disease, overnutrition and upper gastrointestinal disease, and the usual jamboree ("a noisy carousal or merrymaking; an international, or intersectional, gathering of boy scouts").

It is worthy of note that the program has been carefully developed in conjunction with the Massachusetts Academy of General Practice, and that the members of that organization will receive full credit for attendance.

At some time, perhaps, the Assembly may become a function of the Institute, and an American passion for organizational streamlining will be realized.

An anonymous correspondent in New York has addressed a note to the editor, in which he insists that delirium tremens has its origin in the excessive use of cocculus Indicus, which brewers and spirit adulterators introduce extensively into beer and other liquors.

Boston M. and S. J., *October 6, 1852*

BY THE LONDON POST

"DOCTOR" OR "MISTER"?

During a recent visit to the United States I read an article in a well known American magazine in which an author was lamenting the fact that although he held the degree of Ph.D. in one English university, on obtaining an appointment in another English university of equal standing he was denied the title of doctor. Although such a lack of reciprocity must seem hard to understand, at the time I read the article I found the lack of reciprocity between the Baltimore and Ohio Railroad and the Pennsylvania Railroad in the matter of tickets

between Washington and Philadelphia much more irritating. Nevertheless, the method of granting of degrees in British universities is complex, and medical degrees are no exception. Although the British medical student, on passing successfully out of medical school, is regarded as a fully fledged doctor, this is but a courtesy title, for the British universities only confer the degrees of bachelor of medicine and bachelor of surgery on their newly qualified graduates. Thus, in Cambridge the degrees are M.B., B.Chir., in Oxford B.M., B. Ch., in London M.B., B.S., and in Scotland M.B., Ch.B. In view of these variations it is perhaps not surprising that generically the holders of such qualifications are known as "doctors." Nevertheless, in the eyes of the older universities these "doctors" are plain "misters" and will be so addressed in any official correspondence until they have acquired the higher medical degree of M.D. This is usually only sought by those wishing to specialize in internal medicine or one of its branches. The method of obtaining the degree varies from one university to another. In some cases it is by examination, but in Oxford and Cambridge the candidate must submit a thesis on a subject of his own choice that has been approved by the university authorities.

Most British internists also become members or fellows of the Royal College of Physicians. Admission to the membership of the College (M.R.C.P.) is granted on examination, whereas election to the fellowship (F.R.C.P.) comes at a later date to members who bring distinction to their profession.

The surgeons of Britain often remain bachelors of medicine although some acquire the exclusive degree of Master of Surgery of their universities by very rigorous examination. All surgeons of standing, however, are either fellows of the Royal College of Surgeons of England (F.R.C.S.)or fellows of the Royal College of Surgeons of Edinburgh (F.R.C.S.E.). Admission to the fellowship is by examination, and once the young surgeon has been elected to one of these coveted fellowships, he has the barbarous habit of renouncing his title of doctor and reverting to plain mister — presumably to identify himself with his barber-surgeon forebears.

In this country, however, no matter what letters one may append after one's name, no one is a legally qualified medical practitioner unless his name appears on the Medical Register kept by the General Medical Council (G.M.C.). This body consists of representatives of the universities and of the Royal Colleges of Surgeons and Physicians, together with a number of persons nominated by the Crown on the advice of the Privy Council and a number of doctors elected by the medical profession. The G.M.C. ensures that there is a minimum standard of medical education and examination requirements. At present, anyone who has passed his final-year examination may become a registered medical practitioner and, if he wishes, may proceed to private practice. As of January 1, 1953, however, a compulsory year of internship is to be introduced before newly qualified graduates will be registered, bringing the practice in this country into line with that in the United States. In addition to keeping a watch over educational standards, the G.M.C. exercises disciplinary control over the profession and has the power to delete practitioners from the Medical Register if they fail to conform to the accepted ethical and moral standards of the profession.

The Shilling Charge

It was on June 1 last that new charges were introduced for some of the benefits of the National Health Service. Prior to that date part payment for spectacles, dentures and surgical appliances was required of the patient, but since June 1 a charge of one shilling has been payable on all prescriptions dispensed under the Service, and part payment for most forms of dental treatment has been required. It is, however, the payment for drugs that has aroused most interest. The prime motive for the charge was, of course, the fact that the national drug bill has increased every year since 1948, when the N.H.S. started. Answering questions in Parliament about the first month's working of the new scheme, the Minister of Health, Mr. Iain MacLeod, said that in general practice there had been a 15 per cent fall in prescribing. In hospitals, where outpatients must pay one shilling for each issue of their drugs but where inpatients continue to receive them free, there had been no decline in prescribing and no special difficulties had been caused by this introduction of charges. War pensioners and persons in receipt of national assistance are exempt from payment, and in an inquiry at three hospitals in the most congested area of London, only 1 patient was reported to have been unable to pay the charge. The method of collection is not yet uniform throughout the country — dispensing chemists are required to collect the shilling on delivering the drugs, dispensing doctors may charge by postage stamp, and some hospitals have introduced slot machines in their outpatient departments that deliver shilling National Health Service prescription stamps.

Sir Hugh Cairns

The news of the death of Sir Hugh Cairns at the early age of fifty-six will be received with regret in many parts of the world. Coming to England from Australia, studying neurosurgery with Harvey Cushing at the Peter Bent Brigham Hospital and returning to England to the London Hospital, he finally established his own unit at Oxford, where he became Nuffield Professor of Surgery at the Radcliffe Infirmary. It will be perhaps for his wartime work on head injuries that he will chiefly be remembered, for in this sphere he must have brought benefit to large numbers of British and Allied servicemen. It was he who established the Head Injuries Hospital at Oxford, where he not only organized the treatment and rehabilitation of long-term cases but also trained neurosurgical teams to work in the forward areas.

He followed Cushing's teaching that the neurosurgeon must be both his own neurologist and his own neuropathologist, and his more recent contributions on the operation of prefrontal leukotomy and on the streptomycin treatment of tuberculous meningitis have reflected this approach.

The death of this man, who had such a dynamic and yet at the same time such a charming personality, leaves a gap that it will be hard to fill.

John Lister, M.D.

London

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONFERENCE ON HEALTH LEGISLATION

On October 10, 1952, at 10:00 a.m., in the State House, the Massachusetts Central Health Council and the Massachusetts Department of Public Health will jointly sponsor the Ninth Annual Legislative Conference. Health legislation for the coming year will be discussed at this general meeting. In addition to specific bills it is expected that consideration will be given to changes in existing law that should be sought in future years.

Among the member organizations of the Central Health Council are the Massachusetts Medical Society and its Woman's Auxiliary; Massachusetts Department of Public Health; Massachusetts Dental Society; Massachusetts Public Health Association; Massachusetts Tuberculosis and Health League; and Massachusetts State Nurses Association.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Bibliography of Articles on the History of American Medicine, Compiled from "Writings on American History." 1902–1937. By Judson B. Gilbert, M.D. 8°, paper, 44 pp. New York: New York Academy of Medicine, 1951. $1.25.

This list on the history of American medicine is supplementary to the *Bibliography of the History of Medicine of the United States and Canada*, published annually in the *Bulletin of the History of Medicine*. The material is compiled mostly from nonmedical sources. The pamphlet should be found in all history collections.

Topographische Ausdrutung der Bronchien im Röntgenbild mit Berücksichtigung der neuzeitlichen Nomenklatur. Von Priv.-Doz. Dr. Claus Esser, Mainz. F°, paper, 152 pp., with 77 illustrations. Stuttgart: Georg Thieme, 1951. Kartoniert DM 33.– Fortschritte auf dem Gebiete der Röntgenstrahlen vereinigt mit Röntgenpraxis. Ergänzungsband 66. Distributed by Grune & Stratton, Inc., New York, New York.

This monograph deals with the topographical interpretations of the roentgenogram of the bronchi, with special reference to the new nomenclature. The plates are excellent and there is a bibliography appended to the text.

Liver Disease. Consulting editor, Sheila Sherlock, M.D., F.R.C.P. Editor for the Ciba Foundation, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. 8°, cloth, 249 pp., with 112 illustrations. Philadelphia: The Blakiston Company, 1951. $5.00. (A Ciba Foundation Symposium.)

This volume contains the various papers read at the international conference on liver disease, held in London in 1950. The subjects covered included protein metabolism, the etiology of hepatic cirrhosis, portal hypertension and ascites, pigment metabolism, splanchnic blood flow and infectious aspects of liver disease. The small book is well published and there is a good index.

NOTICES

MASSACHUSETTS DEPARTMENT OF MENTAL HEALTH POSTGRADUATE SEMINAR IN NEUROLOGY AND PSYCHIATRY

A review course in basic neurology and psychiatry, under the auspices of the Metropolitan State Hospital and the Psychiatric Training Faculty of Massachusetts Incorporated, will be presented every Monday from 2:00 to 8:30 p.m. from October 6 to December 8, 1952, and from March 2 to May 4, 1953, at the Metropolitan State Hospital, 475 Trapelo Road, Waltham.

All graduate physicians interested in the course, which will consist of seventy lectures should apply to Dr. William C. Gaebler, superintendent, Metropolitan State Hospital, Waltham.

A course in child psychiatry (pediatric neuropsychiatry) consisting of eighteen lectures, will be held at the Walter E. Fernald State School, Waverly, on Tuesdays from October 7 to December 9, 1952, from 6 to 9:30 p.m.

All interested should apply to Dr. Malcolm J. Farrell, Walter E. Fernald State School, Waverley.

MASSACHUSETTS CHAPTER, MULTIPLE SCLEROSIS SOCIETY

A meeting of the Massachusetts Chapter, Multiple Sclerosis Society, will be held on Tuesday, October 7, in the John Hancock Building (Dorothy Quincy Room), Boston. All persons interested in the subject, both medical and nonmedical, are invited.

NEW ENGLAND PATHOLOGICAL SOCIETY

The first fall meeting of the New England Pathological Society will be held at the Massachusetts Memorial Hospitals on Thursday, October 30. A slide seminar will be presented at 4:00 p.m., and there will be an evening program of speakers, beginning at 7:45 p.m.

(*Notices concluded on page xiii*)